

ehp | CHILDREN'S HEALTH COLLECTION 2014

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OCTOBER 2013–SEPTEMBER 2014

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Disease Outcomes

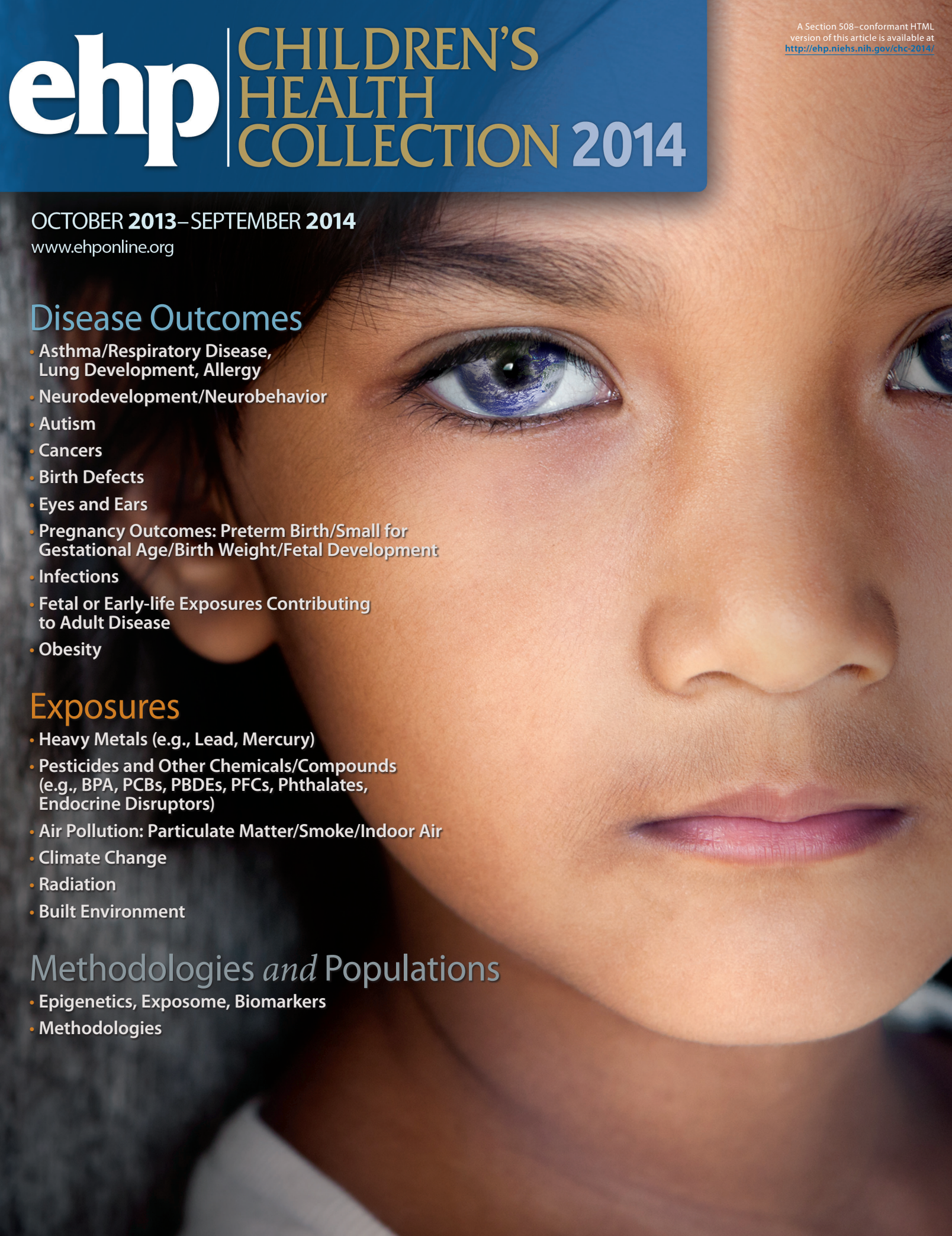
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- Epigenetics, Exposome, Biomarkers
- Methodologies



PREFACE

Children's Health Collection 2014 comprises abstracts of all relevant articles published in *EHP* from October 2013 through September 2014: peer-reviewed research articles, news features, Science Selections, and editorials. Abstracts are featured for each research article, and hyperlinks take readers directly to the full article online (<http://www.ehponline.org/>). The Science Selections are noted just below the related research.

As in previous Collections, the three main sections—Disease Outcomes, Exposures, and Methodologies and Populations—contain all research that has appeared in the Children's Health section of each *EHP* issue as well as relevant reviews and commentaries, research that involves both adult and child cohorts and both animal and human components, adult diseases with fetal or childhood origins, experimental models with direct application to children's health, and topics of general interest to children's health researchers and advocates. Some specific topics (e.g., Built Environment, Climate Change) are featured in news articles but not research.

In this Collection, air pollutants, heavy metals, and chemical compounds continue to be heavily represented in the research, with a wide variety of outcomes (e.g., lung disfunction, congenital anomalies, developmental and behavioral issues, hormone levels) and modes of transfer (e.g., placenta, breast milk, diet, air, soil). A new category is Eyes and Ears, which reflects increased interest in the role of noise pollution in disease and hearing loss. In addition to single longitudinal birth cohorts, larger studies that combine multiple cohorts (e.g., ESCAPE, HELIX, NewGeneris) contribute databases, methodologies, and analyses of multiple environmental factors and outcomes.

Please see <http://www.ehponline.org/collections/> for all the yearly Children's Health collections.



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Air Pollution Exposure and Lung Function in Children: The ESCAPE Project

Ulrike Gehring, Olena Gruzieva, Raymond M. Agius, Rob Beelen, Adnan Custovic, Josef Cyrys, Marloes Eeftens, Claudia Flexeder, Elaine Fuertes, Joachim Heinrich, Barbara Hoffmann, Johan C. de Jongste, Marjan Kerkhof, Claudia Klümper, Michal Korek, Anna Mölter, Erica S. Schultz, Angela Simpson, Dorothea Sugiri, Magnus Svartengren, Andrea von Berg, Alet H. Wijga, Göran Pershagen, and Bert Brunekreef

121:1357–1364 (November–December 2013)
<http://dx.doi.org/10.1289/ehp.1306770>

Background: There is evidence for adverse effects of outdoor air pollution on lung function of children. Quantitative summaries of the effects of air pollution on lung function, however, are lacking due to large differences among studies.

Objectives: We aimed to study the association between residential exposure to air pollution and lung function in five European birth cohorts with a standardized exposure assessment following a common protocol.

Methods: As part of the European Study of Cohorts for Air Pollution Effects (ESCAPE) we analyzed data from birth cohort studies situated in Germany, Sweden, the Netherlands, and the United Kingdom that measured lung function at 6–8 years of age ($n = 5,921$). Annual average exposure to air pollution [nitrogen oxides (NO_2 , NO_x), mass concentrations of particulate matter with diameters < 2.5 , < 10 , and $2.5\text{--}10\text{ }\mu\text{m}$ ($\text{PM}_{2.5}$, PM_{10} , and $\text{PM}_{\text{coarse}}$), and $\text{PM}_{2.5}$ absorbance] at the birth address and current address was estimated by land-use regression models. Associations of lung function with estimated air pollution levels and traffic indicators were estimated for each cohort using linear regression analysis, and then combined by random effects meta-analysis.

Results: Estimated levels of NO_2 , NO_x , $\text{PM}_{2.5}$ absorbance, and $\text{PM}_{2.5}$ at the current address, but not at the birth address, were associated with small decreases in lung function. For example, changes in forced expiratory volume in 1 sec (FEV_1) ranged from -0.86% (95% CI: -1.48 , -0.24%) for a $20\text{-}\mu\text{g}/\text{m}^3$ increase in NO_x to -1.77% (95% CI: -3.34 , -0.18%) for a $5\text{-}\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$.

Conclusions: Exposure to air pollution may result in reduced lung function in schoolchildren.

» NEWS | SCIENCE SELECTION

Small Changes, Big Impact: Exposure to Air Pollution and Reduced Lung Function in Children

Julia R. Barrett | 121:A341 (November–December 2013)
<http://dx.doi.org/10.1289/ehp.121-A341>

Air Pollution and Respiratory Infections during Early Childhood: An Analysis of 10 European Birth Cohorts within the ESCAPE Project

Elaina A. MacIntyre, Ulrike Gehring, Anna Mölter, Elaine Fuertes, Claudia Klümper, Ursula Krämer, Ulrich Quass, Barbara Hoffmann, Mireia Gascon, Bert Brunekreef, Gerard H. Koppelman, Rob Beelen, Gerard Hoek, Matthias Birk, Johan C. de Jongste, H.A. Smit, Josef Cyrys, Olena Gruzieva, Michal Korek, Anna Bergström, Raymond M. Agius, Frank de Vocht, Angela Simpson, Daniela Porta, Francesco Forastiere, Chiara Badaloni, Giulia Cesarini, Ana Esplugues, Ana Fernández-Somoano, Aitana Lerxundi, Jordi Sunyer, Marta Cirach, Mark J. Nieuwenhuijsen, Göran Pershagen, and Joachim Heinrich

122:107–113 (January 2014)
<http://dx.doi.org/10.1289/ehp.1306755>

Background: Few studies have investigated traffic-related air pollution as a risk factor for respiratory infections during early childhood.

Objectives: We aimed to investigate the association between air pollution and pneumonia, croup, and otitis media in 10 European birth cohorts—BAMSE (Sweden), GASPII (Italy), GINIplus and LISAPLUS (Germany), MAAS (United Kingdom), PIAMA (the Netherlands), and four INMA cohorts (Spain)—and to derive combined effect estimates using meta-analysis.

Methods: Parent report of physician-diagnosed pneumonia, otitis media, and croup during early childhood were assessed in relation to annual average pollutant levels [nitrogen dioxide (NO_2), nitrogen oxide (NO_x), particulate matter $\leq 2.5\text{ }\mu\text{m}$ ($\text{PM}_{2.5}$), $\text{PM}_{2.5}$ absorbance, PM_{10} , $\text{PM}_{2.5\text{--}10}$ (coarse PM)], which were estimated using land use regression models and assigned to children based on their residential address at birth. Identical protocols were used to develop regression models for each study area as part of the ESCAPE project. Logistic regression was used to calculate adjusted effect estimates for each study, and random-effects meta-analysis was used to calculate combined estimates.

Results: For pneumonia, combined adjusted odds ratios (ORs) were elevated and statistically significant for all pollutants except $\text{PM}_{2.5}$ (e.g., OR = 1.30; 95% CI: 1.02, 1.65 per $10\text{-}\mu\text{g}/\text{m}^3$ increase in NO_2 and OR = 1.76; 95% CI: 1.00, 3.09 per $10\text{-}\mu\text{g}/\text{m}^3$ PM_{10}). For otitis media and croup, results were generally null across all analyses except for NO_2 and otitis media (OR = 1.09; 95% CI: 1.02, 1.16 per $10\text{-}\mu\text{g}/\text{m}^3$).

Conclusion: Our meta-analysis of 10 European birth cohorts within the ESCAPE project found consistent evidence for an association between air pollution and pneumonia in early childhood, and some evidence for an association with otitis media.

GSTP1 and TNF Gene Variants and Associations between Air Pollution and Incident Childhood Asthma: The Traffic, Asthma and Genetics (TAG) Study

Elaina A. MacIntyre, Michael Brauer, Erik Melén, Carl Peter Bauer, Mario Bauer, Dietrich Berdel, Anna Bergström, Bert Brunekreef, Moira Chan-Yeung, Claudia Klümper, Elaine Fuertes, Ulrike Gehring, Anna Gref, Joachim Heinrich, Olf Herbarth, Marjan Kerkhof, Gerard H. Koppelman, Anita L. Kozyrskyj, Göran Pershagen, Dirkje S. Postma, Elisabeth Thiering, Carla M.T. Tiesler, and Christopher Carlsten, for the TAG Study Group

122:418–424 (April 2014)
<http://dx.doi.org/10.1289/ehp.1307459>

Background: Genetics may partially explain observed heterogeneity in associations between traffic-related air pollution and incident asthma.

Objective: Our aim was to investigate the impact of gene variants associated with oxidative stress and inflammation on associations between air pollution and incident childhood asthma.

Methods: Traffic-related air pollution, asthma, wheeze, gene variant, and potential confounder data were pooled across six birth cohorts. Parents reported physician-diagnosed asthma and wheeze from birth to 7–8 years of age (confirmed by pediatric allergist in two cohorts). Individual estimates of annual average air pollution [nitrogen dioxide (NO₂), particulate matter ≤ 2.5 μm (PM_{2.5}), PM_{2.5} absorbance, ozone] were assigned to each child's birth address using land use regression, atmospheric modeling, and ambient monitoring data. Effect modification by variants in *GSTP1* (rs1138272/Ala¹¹⁴Val and rs1695/Ile¹⁰⁵Val) and *TNF* (rs1800629/G-308A) was investigated.

Results: Data on asthma, wheeze, potential confounders, at least one SNP of interest, and NO₂ were available for 5,115 children. *GSTP1* rs1138272 and *TNF* rs1800629 SNPs were associated with asthma and wheeze, respectively. In relation to air pollution exposure, children with one or more *GSTP1* rs1138272 minor allele were at increased risk of current asthma [odds ratio (OR) = 2.59; 95% CI: 1.43, 4.68 per 10 μg/m³ NO₂] and ever asthma (OR = 1.64; 95% CI: 1.06, 2.53) compared with homozygous major allele carriers (OR = 0.95; 95% CI: 0.68, 1.32 for current and OR = 1.20; 95% CI: 0.98, 1.48 for ever asthma; Bonferroni-corrected interaction *p* = 0.04 and 0.01, respectively). Similarly, for *GSTP1* rs1695, associations between NO₂ and current and ever asthma had ORs of 1.43 (95% CI: 1.03, 1.98) and 1.36 (95% CI: 1.08, 1.70), respectively, for minor allele carriers compared with ORs of 0.82 (95% CI: 0.52, 1.32) and 1.12 (95% CI: 0.84, 1.49) for homozygous major allele carriers (Bonferroni-corrected interaction *p*-values 0.48 and 0.09). There were no clear differences by *TNF* genotype.

Conclusions: Children carrying *GSTP1* rs1138272 or rs1695 minor alleles may constitute a susceptible population at increased risk of asthma associated with air pollution.

Influence of Urbanicity and County Characteristics on the Association between Ozone and Asthma Emergency Department Visits in North Carolina

Jason D. Sacks, Ana G. Rappold, J. Allen Davis Jr., David B. Richardson, Anna E. Waller, and Thomas J. Luben

122:506–512 (May 2014)
<http://dx.doi.org/10.1289/ehp.1306940>

Background: Air pollution epidemiologic studies, often conducted in large metropolitan areas because of proximity to regulatory monitors, are limited in their ability to examine potential associations between air pollution exposures and health effects in rural locations.

Methods: Using a time-stratified case-crossover framework, we examined associations between asthma emergency department (ED) visits in North Carolina (2006–2008), collected by a surveillance system, and short-term ozone (O₃) exposures using predicted concentrations from the Community Multiscale Air Quality (CMAQ) model. We estimated associations by county groupings based on four urbanicity classifications (representative of county size and urban proximity) and county health.

Results: O₃ was associated with asthma ED visits in all-year and warm season (April–October) analyses [odds ratio (OR) = 1.019; 95% CI: 0.998, 1.040; OR = 1.020; 95% CI: 0.997, 1.044, respectively, for a 20-ppb increase in lag 0–2 days O₃]. The association was strongest in Less Urbanized counties, with no evidence of a positive association in Rural counties. Associations were similar when adjusted for fine particulate matter in copollutant models. Associations were stronger for children (5–17 years of age) compared with other age groups, and for individuals living in counties identified with poorer health status compared with counties that had the highest health rankings, although estimated associations for these subgroups had larger uncertainty.

Conclusions: Associations between short-term O₃ exposures and asthma ED visits differed by overall county health and urbanicity, with stronger associations in Less Urbanized counties, and no positive association in Rural counties. Results also suggest that children are at increased risk of O₃-related respiratory effects.

NEURODEVELOPMENT/NEUROBEHAVIOR

Domain-Specific Effects of Prenatal Exposure to PCBs, Mercury, and Lead on Infant Cognition: Results from the Environmental Contaminants and Child Development Study in Nunavik

Olivier Boucher, Gina Muckle, Joseph L. Jacobson, R. Colin Carter, Melissa Kaplan-Estrin, Pierre Ayotte, Éric Dewailly, and Sandra W. Jacobson

122:310–316 (March 2014)

<http://dx.doi.org/10.1289/ehp.1206323>

Background: Polychlorinated biphenyls (PCBs), methylmercury (MeHg), and lead (Pb) are environmental contaminants known for their adverse effects on cognitive development.

Objectives: In this study we examined the effects of prenatal exposure to PCBs, MeHg, and Pb on cognitive development in a sample of Inuit infants from Arctic Québec.

Methods: Mothers were recruited at local prenatal clinics. PCBs, mercury (Hg), Pb, and two seafood nutrients—docosahexaenoic acid (DHA) and selenium (Se)—were measured in umbilical cord blood. Infants ($n = 94$) were assessed at 6.5 and 11 months of age on the Fagan Test of Infant Intelligence (FTII), A-not-B test, and Bayley Scales of Infant Development–2nd Edition (BSID-II).

Results: Multiple regression analyses revealed that higher prenatal PCB exposure was associated with decreased FTII novelty preference, indicating impaired visual recognition memory. Prenatal Hg was associated with poorer performance on A-not-B, which depends on working memory and is believed to be a precursor of executive function. Prenatal Pb was related to longer FTII fixation durations, indicating slower speed of information processing.

Conclusions: PCBs, MeHg, and Pb each showed specific and distinct patterns of adverse associations with the outcomes measured during infancy. By contrast, none of these exposures was associated with performance on the BSID-II, a global developmental measure. The more focused, narrow band measures of cognitive function that appeared to be sensitive to these exposures also provide early indications of long-term impairment in specific domains that would otherwise not likely be evident until school age.

Prenatal Phthalate Exposures and Neurobehavioral Development Scores in Boys and Girls at 6–10 Years of Age

Roni W. Kobrosly, Sarah Evans, Amir Miodovnik, Emily S. Barrett, Sally W. Thurston, Antonia M. Calafat, and Shanna H. Swan

122:521–528 (May 2014)

<http://dx.doi.org/10.1289/ehp.1307063>

Background: There is concern over potential neurobehavioral effects of prenatal phthalate exposures, but available data are inconsistent.

Objectives: We examined associations between prenatal urinary concentrations of phthalate metabolites and neurobehavioral scores among children.

Methods: We measured phthalate metabolite concentrations in urine samples from 153 pregnant participants in the Study for Future Families, a multicenter cohort study. Mothers completed the Child Behavior Checklist when the children were 6–10 years of age. We estimated overall and sex-specific associations between phthalate concentrations and behavior using adjusted multiple regression interaction models.

Results: In boys, concentrations of monoisobutyl phthalate were associated with higher scores for inattention ($\beta = 0.27$; 95% CI: 0.04, 0.50), rule-breaking behavior ($\beta = 0.20$; 95% CI: 0.01, 0.38), aggression ($\beta = 0.34$; 95% CI: 0.09, 0.59), and conduct problems ($\beta = 0.39$; 95% CI: 0.20, 0.58), whereas the molar sum of di(2-ethylhexyl) phthalate metabolites was associated with higher scores for somatic problems ($\beta = 0.15$; 95% CI: 0.03, 0.28). Higher monobenzyl phthalate concentrations were associated with higher scores for oppositional behavior ($\beta = 0.16$; 95% CI: 0.01, 0.32) and conduct problems ($\beta = 0.21$; 95% CI: 0.06, 0.37) in boys, but with reduced anxiety scores in girls ($\beta = -0.20$; 95% CI: -0.39 , -0.01). In general, the associations reported above were close to the null among girls. Model coefficients represent the difference in the square root–transformed outcome score associated with a 1-unit increase in log-transformed metabolites.

Conclusions: Our results suggest associations between exposure to certain phthalates in late pregnancy and behavioral problems in boys. Given the few studies on this topic and methodological and population differences among studies, additional research is warranted.

Prenatal Polybrominated Diphenyl Ether Exposures and Neurodevelopment in U.S. Children through 5 Years of Age: The HOME Study

Aimin Chen, Kimberly Yolton, Stephen A. Rauch, Glenys M. Webster, Richard Hornung, Andreas Sjödin, Kim N. Dietrich, and Bruce P. Lanphear

122:856–862 (August 2014)
<http://dx.doi.org/10.1289/ehp.1307562>

Background: Polybrominated diphenyl ethers (PBDEs) are persistent chemicals that have been widely used as flame retardants in furniture, carpet padding, car seats, and other consumer products during the past three decades.

Objective: We examined whether *in utero* exposure to PBDEs is associated with child cognitive function and behavior in a U.S. study sample.

Methods: In a prospective birth cohort, we measured maternal serum concentrations of BDE-47 and other PBDE congeners in 309 women at 16 weeks of gestation during 2003–2006 and followed their children in Cincinnati, Ohio. We measured cognitive and motor abilities using the Bayley Scales of Infant Development-II at ages 1, 2, and 3 years; intelligence using the Wechsler Preschool and Primary Scale of Intelligence-III at age 5 years; and children's behaviors using the Behavioral Assessment System for Children-2 annually at ages 2–5 years. We used linear mixed models or generalized estimating equations with adjustment for potential confounders to estimate associations between these outcomes and \log_{10} -transformed PBDE concentrations.

Results: The geometric mean of BDE-47 in maternal serum (20.1 ng/g lipid) was comparable with U.S. adult national reference values. Prenatal BDE-47 was not significantly associated with Bayley Mental or Psychomotor Development Indices at 1–3 years, but a 10-fold increase in prenatal BDE-47 was associated with a 4.5-point decrease (95% CI: –8.8, –0.1) in Full-Scale IQ and a 3.3-point increase (95% CI: 0.3, 6.3) in the hyperactivity score at age 5 years.

Conclusions: Prenatal exposure to PBDEs was associated with lower IQ and higher hyperactivity scores in children.

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More Evidence for PBDEs as Neurotoxins: Cohort Study Corroborates Earlier Findings

Kellyn S. Betts | 122:A221 (August 2014)
<http://dx.doi.org/10.1289/ehp.122-A221>

AUTISM

Gestational Exposure to Endocrine-Disrupting Chemicals and Reciprocal Social, Repetitive, and Stereotypic Behaviors in 4- and 5-Year-Old Children: The HOME Study

Joseph M. Braun, Amy E. Kalkbrenner, Allan C. Just, Kimberly Yolton, Antonia M. Calafat, Andreas Sjödin, Russ Hauser, Glenys M. Webster, Aimin Chen, and Bruce P. Lanphear

122:513–520 (May 2014)
<http://dx.doi.org/10.1289/ehp.1307261>

Background: Endocrine-disrupting chemicals (EDCs) may be involved in the etiology of autism spectrum disorders, but identifying relevant chemicals within mixtures of EDCs is difficult.

Objective: Our goal was to identify gestational EDC exposures associated with autistic behaviors.

Methods: We measured the concentrations of 8 phthalate metabolites, bisphenol A, 25 polychlorinated biphenyls (PCBs), 6 organochlorine pesticides, 8 brominated flame retardants, and 4 perfluoroalkyl substances in blood or urine samples from 175 pregnant women in the HOME (Health Outcomes and Measures of the Environment) Study (Cincinnati, OH). When children were 4 and 5 years old, mothers completed the Social Responsiveness Scale (SRS), a measure of autistic behaviors. We examined confounder-adjusted associations between 52 EDCs and SRS scores using a two-stage hierarchical analysis to account for repeated measures and confounding by correlated EDCs.

Results: Most of the EDCs were associated with negligible absolute differences in SRS scores (≤ 1.5). Each 2-SD increase in serum concentrations of polybrominated diphenyl ether-28 (PBDE-28) ($\beta = 2.5$; 95% CI: –0.6, 5.6) or *trans*-nonachlor ($\beta = 4.1$; 95% CI: 0.8–7.3) was associated with more autistic behaviors. In contrast, fewer autistic behaviors were observed among children born to women with detectable versus nondetectable concentrations of PCB-178 ($\beta = -3.0$; 95% CI: –6.3, 0.2), β -hexachlorocyclohexane ($\beta = -3.3$; 95% CI: –6.1, –0.5), or PBDE-85 ($\beta = -3.2$; 95% CI: –5.9, –0.5). Increasing perfluorooctanoate (PFOA) concentrations were also associated with fewer autistic behaviors ($\beta = -2.0$; 95% CI: –4.4, 0.4).

Conclusions: Some EDCs were associated with autistic behaviors in this cohort, but our modest sample size precludes us from dismissing chemicals with null associations. PFOA, β -hexachlorocyclohexane, PCB-178, PBDE-28, PBDE-85, and *trans*-nonachlor deserve additional scrutiny as factors that may be associated with childhood autistic behaviors.

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Clues to Autistic Behaviors: Exploring the Role of Endocrine Disruptors

Kellyn S. Betts | 122:A137 (May 2014)
<http://dx.doi.org/10.1289/ehp.122-A137>

CANCERS

Domestic Radon Exposure and Risk of Childhood Cancer: A Prospective Census-Based Cohort Study

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121:1239–1244 (October 2013)
<http://dx.doi.org/10.1289/ehp.1306500>

Background: In contrast with established evidence linking high doses of ionizing radiation with childhood cancer, research on low-dose ionizing radiation and childhood cancer has produced inconsistent results.

Objective: We investigated the association between domestic radon exposure and childhood cancers, particularly leukemia and central nervous system (CNS) tumors.

Methods: We conducted a nationwide census-based cohort study including all children < 16 years of age living in Switzerland on 5 December 2000, the date of the 2000 census. Follow-up lasted until the date of diagnosis, death, emigration, a child's 16th birthday, or 31 December 2008. Domestic radon levels were estimated for each individual home address using a model developed and validated based on approximately 45,000 measurements taken throughout Switzerland. Data were analyzed with Cox proportional hazard models adjusted for child age, child sex, birth order, parents' socioeconomic status, environmental gamma radiation, and period effects.

Results: In total, 997 childhood cancer cases were included in the study. Compared with children exposed to a radon concentration below the median (< 77.7 Bq/m³), adjusted hazard ratios for children with exposure ≥ the 90th percentile (≥ 139.9 Bq/m³) were 0.93 (95% CI: 0.74, 1.16) for all cancers, 0.95 (95% CI: 0.63, 1.43) for all leukemias, 0.90 (95% CI: 0.56, 1.43) for acute lymphoblastic leukemia, and 1.05 (95% CI: 0.68, 1.61) for CNS tumors.

Conclusions: We did not find evidence that domestic radon exposure is associated with childhood cancer, despite relatively high radon levels in Switzerland.

Childhood Cancer and Traffic-Related Air Pollution Exposure in Pregnancy and Early Life

Julia E. Heck, Jun Wu, Christina Lombardi, Jiaheng Qiu, Travis J. Meyers, Michelle Wilhelm, Myles Cockburn, and Beate Ritz

121:1385–1391 (November–December 2013)
<http://dx.doi.org/10.1289/ehp.1306761>

Background: The literature on traffic-related air pollution and childhood cancers is inconclusive, and little is known on rarer cancer types.

Objectives: We sought to examine associations between childhood cancers and traffic-related pollution exposure.

Methods: The present study included children < 6 years of age identified in the California Cancer Registry (born 1998–2007) who could be linked to a California birth certificate ($n = 3,590$). Controls were selected at random from California birthrolls ($n = 80,224$). California LINE Source Dispersion Modeling, version 4 (CALINE4) was used to generate estimates of local traffic exposures for each trimester of pregnancy and in the first year of life at the address indicated on the birth certificate. We checked our findings by additionally examining associations with particulate matter ($\leq 2.5 \mu\text{m}$ in aerodynamic diameter; $\text{PM}_{2.5}$) pollution measured by community-based air pollution monitors, and with a simple measure of traffic density.

Results: With unconditional logistic regression, a per interquartile range increase in exposure to traffic-related pollution during the first trimester (0.0538 ppm carbon monoxide, estimated using CALINE4) was associated with acute lymphoblastic leukemia [ALL; first trimester odds ratio (OR) = 1.05; 95% CI: 1.01, 1.10]; germ cell tumors (OR = 1.16; 95% CI: 1.04, 1.29), particularly teratomas (OR = 1.26; 95% CI: 1.12, 1.41); and retinoblastoma (OR = 1.11; 95% CI: 1.01, 1.21), particularly bilateral retinoblastoma (OR = 1.16; 95% CI: 1.02, 1.33). Retinoblastoma was also associated with average $\text{PM}_{2.5}$ concentrations during pregnancy, and ALL and teratomas were associated with traffic density near the child's residence at birth.

Conclusions: We estimated weak associations between early exposure to traffic pollution and several childhood cancers. Because this is the first study to report on traffic pollution in relation to retinoblastoma or germ cell tumors, and both cancers are rare, these findings require replication in other studies.

BIRTH DEFECTS

Anogenital Distance and Penile Length in Infants with Hypospadias or Cryptorchidism: Comparison with Normative Data

Ajay Thankamony, Ngee Lek, Dan Carroll, Martyn Williams, David B. Dunger, Carlo L. Acerini, Ken K. Ong, and Ieuan A. Hughes

122:207–211 (February 2014)

<http://dx.doi.org/10.1289/ehp.1307178>

Background: Anogenital distance (AGD) in animals is a sensitive biomarker of fetal endocrine disruption and the associated testicular dysgenesis syndrome (TDS). However, AGD in human infants with cryptorchidism and hypospadias, which are potential manifestations of TDS during childhood, is not clearly described.

Objective: Our aim was to compare AGD in boys with cryptorchidism or hypospadias against normative data.

Methods: Boys with isolated cryptorchidism ($n = 71$, age 13.4 ± 5.8 months) or hypospadias ($n = 81$, age 11.4 ± 6.2 months) were recruited from a tertiary center for measurement of AGD and penile length; they were compared with 487 healthy full-term boys from a birth cohort by deriving age-specific standard deviation scores (SDS).

Results: Boys with cryptorchidism were older ($p = 0.048$) compared with boys with hypospadias. Boys with hypospadias had shorter mean AGD and penile length SDS than healthy boys (both $p < 0.0001$). Mean AGD and penile length SDS values in boys with cryptorchidism were longer than mean values in boys with hypospadias (both $p < 0.01$) and shorter than mean values in healthy boys (both $p < 0.0001$). Mean penile length SDS decreased as the severity of hypospadias increased ($p_{\text{trend}} = 0.078$).

Conclusions: In the study population, AGD and penile length were reduced in boys with hypospadias or cryptorchidism relative to normative data derived from a longitudinal birth cohort. The findings support the use of AGD as a quantitative biomarker to examine the prenatal effects of exposure to endocrine disruptors on the development of the male reproductive tract.

Traffic-Related Air Pollution and Congenital Anomalies in Barcelona

Anna Schembari, Mark J. Nieuwenhuijsen, Joaquin Salvador, Audrey de Nazelle, Marta Cirach, Payam Dadvand, Rob Beelen, Gerard Hoek, Xavier Basagaña, and Martine Vrijheid

122:317–323 (March 2014)

<http://dx.doi.org/10.1289/ehp.1306802>

Background: A recent meta-analysis suggested evidence for an effect of exposure to ambient air pollutants on risk of certain congenital heart defects. However, few studies have investigated the effects of traffic-related air pollutants with sufficient spatial accuracy.

Objectives: We estimated associations between congenital anomalies and exposure to traffic-related air pollution in Barcelona, Spain.

Method: Cases with nonchromosomal anomalies ($n = 2,247$) and controls ($n = 2,991$) were selected from the Barcelona congenital anomaly register during 1994–2006. Land use regression models from the European Study of Cohorts for Air Pollution Effects (ESCAPE), were applied to residential addresses at birth to estimate spatial exposure to nitrogen oxides and dioxide (NO_x , NO_2), particulate matter with diameter $\leq 10 \mu\text{m}$ (PM_{10}), 10 – $2.5 \mu\text{m}$ ($\text{PM}_{\text{coarse}}$), $\leq 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$), and $\text{PM}_{2.5}$ absorbance. Spatial estimates were adjusted for temporal trends using data from routine monitoring stations for weeks 3–8 of each pregnancy. Logistic regression models were used to calculate odds ratios (ORs) for 18 congenital anomaly groups associated with an interquartile-range (IQR) increase in exposure estimates.

Results: In spatial and spatiotemporal exposure models, we estimated statistically significant associations between an IQR increase in NO_2 ($12.2 \mu\text{g}/\text{m}^3$) and coarctation of the aorta ($\text{OR}_{\text{spatiotemporal}} = 1.15$; 95% CI: 1.01, 1.31) and digestive system defects ($\text{OR}_{\text{spatiotemporal}} = 1.11$; 95% CI: 1.00, 1.23), and between an IQR increase in $\text{PM}_{\text{coarse}}$ ($3.6 \mu\text{g}/\text{m}^3$) and abdominal wall defects ($\text{OR}_{\text{spatiotemporal}} = 1.93$; 95% CI: 1.37, 2.73). Other statistically significant increased and decreased ORs were estimated based on the spatial model only or the spatiotemporal model only, but not both.

Conclusions: Our results overall do not indicate an association between traffic-related air pollution and most groups of congenital anomalies. Findings for coarctation of the aorta are consistent with those of the previous meta-analysis.

Birth Outcomes and Maternal Residential Proximity to Natural Gas Development in Rural Colorado

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122:412–417 (April 2014)

<http://dx.doi.org/10.1289/ehp.1306722>

Background: Birth defects are a leading cause of neonatal mortality. Natural gas development (NGD) emits several potential teratogens, and U.S. production of natural gas is expanding.

Objectives: We examined associations between maternal residential proximity to NGD and birth outcomes in a retrospective cohort study of 124,842 births between 1996 and 2009 in rural Colorado.

Methods: We calculated inverse distance weighted natural gas well counts within a 10-mile radius of maternal residence to estimate maternal exposure to NGD. Logistic regression, adjusted for maternal and infant covariates, was used to estimate associations with exposure tertiles for congenital heart defects (CHDs), neural tube defects (NTDs), oral clefts, preterm birth, and term low birth weight. The association with term birth weight was investigated using multiple linear regression.

Results: Prevalence of CHDs increased with exposure tertile, with an odds ratio (OR) of 1.3 for the highest tertile (95% CI: 1.2, 1.5); NTD prevalence was associated with the highest tertile of exposure (OR = 2.0; 95% CI: 1.0, 3.9, based on 59 cases), compared with the absence of any gas wells within a 10-mile radius. Exposure was negatively associated with preterm birth and positively associated with fetal growth, although the magnitude of association was small. No association was found between exposure and oral clefts.

Conclusions: In this large cohort, we observed an association between density and proximity of natural gas wells within a 10-mile radius of maternal residence and prevalence of CHDs and possibly NTDs. Greater specificity in exposure estimates is needed to further explore these associations.

» NEWS | SCIENCE SELECTION

Birth Defects and Mothers' Proximity to Natural Gas Development: Is There a Connection?

Lindsey A. Konkel | 122:A109 (April 2014)

<http://dx.doi.org/10.1289/ehp.122-A109>

Maternal Exposure to Criteria Air Pollutants and Congenital Heart Defects in Offspring: Results from the National Birth Defects Prevention Study

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122:863–872 (August 2014)

<http://dx.doi.org/10.1289/ehp.1307289>

Background: Epidemiologic literature suggests that exposure to air pollutants is associated with fetal development.

Objectives: We investigated maternal exposures to air pollutants during weeks 2–8 of pregnancy and their associations with congenital heart defects.

Methods: Mothers from the National Birth Defects Prevention Study, a nine-state case–control study, were assigned 1-week and 7-week averages of daily maximum concentrations of carbon monoxide, nitrogen dioxide, ozone, and sulfur dioxide and 24-hr measurements of fine and coarse particulate matter using the closest air monitor within 50 km to their residence during early pregnancy. Depending on the pollutant, a maximum of 4,632 live-birth controls and 3,328 live-birth, fetal-death, or electively terminated cases had exposure data. Hierarchical regression models, adjusted for maternal demographics and tobacco and alcohol use, were constructed. Principal component analysis was used to assess these relationships in a multipollutant context.

Results: Positive associations were observed between exposure to nitrogen dioxide and coarctation of the aorta and pulmonary valve stenosis. Exposure to fine particulate matter was positively associated with hypoplastic left heart syndrome but inversely associated with atrial septal defects. Examining individual exposure-weeks suggested associations between pollutants and defects that were not observed using the 7-week average. Associations between left ventricular outflow tract obstructions and nitrogen dioxide and between hypoplastic left heart syndrome and particulate matter were supported by findings from the multipollutant analyses, although estimates were attenuated at the highest exposure levels.

Conclusions: Using daily maximum pollutant levels and exploring individual exposure-weeks revealed some positive associations between certain pollutants and defects and suggested potential windows of susceptibility during pregnancy.

EYES AND EARS

Environmental Noise Pollution in the United States: Developing an Effective Public Health Response

Monica S. Hammer, Tracy K. Swinburn, and Richard L. Neitzel

122:115–119 (February 2014)

<http://dx.doi.org/10.1289/ehp.1307272>

Background: Tens of millions of Americans suffer from a range of adverse health outcomes due to noise exposure, including heart disease and hearing loss. Reducing environmental noise pollution is achievable and consistent with national prevention goals, yet there is no national plan to reduce environmental noise pollution.

Objectives: We aimed to describe some of the most serious health effects associated with noise, summarize exposures from several highly prevalent noise sources based on published estimates as well as extrapolations made using these estimates, and lay out proven mechanisms and strategies to reduce noise by incorporating scientific insight and technological innovations into existing public health infrastructure.

Discussion: Approximately 104 million individuals had annual $L_{EQ(24)}$ levels > 70 dBA (equivalent to a continuous average exposure level of > 70 dBA over 24 hr) in 2013 and were at risk of noise-induced hearing loss. Tens of millions more may be at risk of heart disease, and other noise-related health effects. Direct regulation, altering the informational environment, and altering the built environment are the least costly, most logistically feasible, and most effective noise reduction interventions.

Conclusion: Significant public health benefit can be achieved by integrating interventions that reduce environmental noise levels and exposures into the federal public health agenda.

» NEWS | SCIENCE SELECTION

Fighting Noise Pollution: A Public Health Strategy

David C. Holzman | 122:A58 (February 2014)

<http://dx.doi.org/10.1289/ehp.122-A58>

RELATED ARTICLES

NEWS | Myopia: The Evidence for Environmental Factors

Tim Loughheed | 122:A12 (January 2014)

<http://dx.doi.org/10.1289/ehp.122-A12>

Myopia, or nearsightedness, was long blamed on genetics and behavior, but dramatic increases in prevalence in recent decades point to environmental factors as well. Moreover, time spent outdoors appears to have a protective effect against myopia, although investigators still aren't sure why.



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NEWS | Wind Turbines: A Different Breed of Noise?

Nate Seltenrich | 122:A20 (January 2014)

<http://dx.doi.org/10.1289/ehp.122-A20>

Since at least 1930, researchers have amassed a body of evidence on the adverse nonauditory health effects of environmental noise. More recently, a new source of noise has entered the scene: wind turbines. As wind farms become more common near populated areas, researchers are investigating the unique qualities of the noise they produce.

PREGNANCY OUTCOMES: PRETERM BIRTH/SMALL FOR GESTATIONAL AGE/ BIRTH WEIGHT/FETAL DEVELOPMENT

Bulky DNA Adducts in Cord Blood, Maternal Fruit-and-Vegetable Consumption, and Birth Weight in a European Mother–Child Study (NewGeneris)

Marie Pedersen, Bernadette Schoket, Roger W. Godschalk, John Wright, Hans von Stedingk, Margareta Törnqvist, Jordi Sunyer, Jeanette K. Nielsen, Domenico F. Merlo, Michelle A. Mendez, Helle M. Meltzer, Viktória Lukács, Anette Landström, Soterios A. Kyrtopoulos, Katalin Kovács, Lisbeth E. Knudsen, Margaretha Haugen, Laura J. Hardie, Kristine B. Gützow, Sarah Fleming, Eleni Fthenou, Peter B. Farmer, Aina Espinosa, Leda Chatzi, Gunnar Brunborg, Nigel J. Brady, Maria Botsivali, Khelifa Arab, Livia Anna, Jan Alexander, Silvia Agramunt, Jos C. Kleinjans, Dan Segerbäck, and Manolis Kogevinas

121:1200–1206 (October 2013)
<http://dx.doi.org/10.1289/ehp.1206333>

Background: Tobacco-smoke, airborne, and dietary exposures to polycyclic aromatic hydrocarbons (PAHs) have been associated with reduced prenatal growth. Evidence from biomarker-based studies of low-exposed populations is limited. Bulky DNA adducts in cord blood reflect the prenatal effective dose to several genotoxic agents including PAHs.

Objectives: We estimated the association between bulky DNA adduct levels and birth weight in a multicenter study and examined modification of this association by maternal intake of fruits and vegetables during pregnancy.

Methods: Pregnant women from Denmark, England, Greece, Norway, and Spain were recruited in 2006–2010. Adduct levels were measured by the ³²P-postlabeling technique in white blood cells from 229 mothers and 612 newborns. Maternal diet was examined through questionnaires.

Results: Adduct levels in maternal and cord blood samples were similar and positively correlated (median, 12.1 vs. 11.4 adducts in 10⁸ nucleotides; Spearman rank correlation coefficient = 0.66, $p < 0.001$). Cord blood adduct levels were negatively associated with birth weight, with an estimated difference in mean birth weight of –129 g (95% CI: –233, –25 g) for infants in the highest versus lowest tertile of adducts. The negative association with birth weight was limited to births in Norway, Denmark, and England, the countries with the lowest adduct levels, and was more pronounced in births to mothers with low intake of fruits and vegetables (–248 g; 95% CI: –405, –92 g) compared with those with high intake (–58 g; 95% CI: –206, 90 g).

Conclusions: Maternal exposure to genotoxic agents that induce the formation of bulky DNA adducts may affect intrauterine growth. Maternal fruit and vegetable consumption may be protective.

» NEWS | SCIENCE SELECTION

Prenatal Protection: Maternal Diet May Modify Impact of PAHs

Julia R. Barrett | 121:A311 (October 2013)
<http://dx.doi.org/10.1289/ehp.121-A311>

Serum Perfluorooctanoic Acid and Perfluorooctane Sulfonate Concentrations in Relation to Birth Outcomes in the Mid-Ohio Valley, 2005–2010

Lyndsey A. Darrow, Cheryl R. Stein, and Kyle Steenland

121:1207–1213 (October 2013)
<http://dx.doi.org/10.1289/ehp.1206372>

Background: Previous research suggests perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) may be associated with adverse pregnancy outcomes.

Objective: We conducted a population-based study of PFOA and PFOS and birth outcomes from 2005 through 2010 in a Mid-Ohio Valley community exposed to high levels of PFOA through drinking-water contamination.

Methods: Women provided serum for PFOA and PFOS measurement in 2005–2006 and reported reproductive histories in subsequent follow-up interviews. Reported singleton live births among 1,330 women after 1 January 2005 were linked to birth records ($n = 1,630$) to identify the outcomes of preterm birth (< 37 weeks gestation), pregnancy-induced hypertension, low birth weight (< 2,500 g), and birth weight (grams) among full-term infants.

Results: We observed little or no evidence of association between maternal serum PFOA or PFOS and preterm birth ($n = 158$) or low birth weight ($n = 88$). Serum PFOA and PFOS were both positively associated with pregnancy-induced hypertension ($n = 106$), with adjusted odds ratios (ORs) per log unit increase in PFOA and PFOS of 1.27 (95% CI: 1.05, 1.55) and 1.47 (95% CI: 1.06, 2.04), respectively, but associations did not increase monotonically when categorized by quintiles. Results of subanalyses restricted to pregnancies conceived after blood collection were consistent with the main analyses. There was suggestion of a modest negative association between PFOS and birth weight in full-term infants (–29 g per log unit increase; 95% CI: –66, 7), which became stronger when restricted to births conceived after the blood sample collection (–49 g per log unit increase; 95% CI: –90, –8).

Conclusion: Results provide some evidence of positive associations between measured serum perfluorinated compounds and pregnancy-induced hypertension and a negative association between PFOS and birth weight among full-term infants.

Is the Relationship between Prenatal Exposure to PCB-153 and Decreased Birth Weight Attributable to Pharmacokinetics?

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121:1219–1224 (October 2013)
<http://dx.doi.org/10.1289/ehp.1206457>

Background: A recent meta-analysis based on data from > 7,000 pregnancies reported an association between prenatal polychlorinated biphenyl (PCB)-153 exposure and reduced birth weight. Gestational weight gain, which is associated negatively with PCB levels in maternal and cord blood, and positively with birth weight, could substantially confound this association.

Objective: We sought to estimate the influence of gestational weight gain on the association between PCB-153 exposure and birth weight using a pharmacokinetic model.

Methods: We modified a recently published pharmacokinetic model and ran Monte Carlo simulations accounting for variability in physiologic parameters and their correlations. We evaluated the pharmacokinetic model by comparing simulated plasma PCB-153 levels during pregnancy to serial measurements in 10 pregnant women from another study population. We estimated the association between simulated plasma PCB-153 levels and birth weight using linear regression models.

Results: The plasma PCB-153 level profiles generated with the pharmacokinetic model were comparable to measured levels in 10 pregnant women. We estimated a 118-g decrease in birth weight (95% CI: –129, –106 g) for each 1- $\mu\text{g/L}$ increase in simulated cord plasma PCB-153, compared with the 150-g decrease estimated based on the previous meta-analysis. The estimated decrease in birth weight was reduced to –6 g (95% CI: –18, 6 g) when adjusted for simulated gestational weight gain.

Conclusion: Our findings suggest that associations previously noted between PCB levels and birth weight may be attributable to confounding by maternal weight gain during pregnancy.

Outdoor Air Pollution, Preterm Birth, and Low Birth Weight: Analysis of the World Health Organization Global Survey on Maternal and Perinatal Health

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122:425–430 (April 2014)
<http://dx.doi.org/10.1289/ehp.1306837>

Background: Inhaling fine particles (particulate matter with diameter $\leq 2.5 \mu\text{m}$; $\text{PM}_{2.5}$) can induce oxidative stress and inflammation, and may contribute to onset of preterm labor and other adverse perinatal outcomes.

Objectives: We examined whether outdoor $\text{PM}_{2.5}$ was associated with adverse birth outcomes among 22 countries in the World Health Organization Global Survey on Maternal and Perinatal Health from 2004 through 2008.

Methods: Long-term average (2001–2006) estimates of outdoor $\text{PM}_{2.5}$ were assigned to 50-km-radius circular buffers around each health clinic where births occurred. We used generalized estimating equations to determine associations between clinic-level $\text{PM}_{2.5}$ levels and preterm birth and low birth weight at the individual level, adjusting for seasonality and potential confounders at individual, clinic, and country levels. Country-specific associations were also investigated.

Results: Across all countries, adjusting for seasonality, $\text{PM}_{2.5}$ was not associated with preterm birth, but was associated with low birth weight [odds ratio (OR) = 1.22; 95% CI: 1.07, 1.39 for fourth quartile of $\text{PM}_{2.5}$ ($> 20.2 \mu\text{g}/\text{m}^3$) compared with the first quartile ($< 6.3 \mu\text{g}/\text{m}^3$)]. In China, the country with the largest $\text{PM}_{2.5}$ range, preterm birth and low birth weight both were associated with the highest quartile of $\text{PM}_{2.5}$ only, which suggests a possible threshold effect (OR = 2.54; 95% CI: 1.42, 4.55 and OR = 1.99; 95% CI: 1.06, 3.72 for preterm birth and low birth weight, respectively, for $\text{PM}_{2.5} \geq 36.5 \mu\text{g}/\text{m}^3$ compared with $\text{PM}_{2.5} < 12.5 \mu\text{g}/\text{m}^3$).

Conclusions: Outdoor $\text{PM}_{2.5}$ concentrations were associated with low birth weight but not preterm birth. In rapidly developing countries, such as China, the highest levels of air pollution may be of concern for both outcomes.

» NEWS | SCIENCE SELECTION

Apples to Apples: Comparing $\text{PM}_{2.5}$ Exposures and Birth Outcomes in Understudied Countries

Julia R. Barrett | 122:A110 (April 2014)
<http://dx.doi.org/10.1289/ehp.122-A110>

Gestational Weight Gain and Exposure of Newborns to Persistent Organic Pollutants

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122:873–879 (August 2014)
<http://dx.doi.org/10.1289/ehp.1306758>

Background: Exposure to persistent organic pollutants (POPs) during fetal development can increase the risk of adverse health effects during childhood. Maternal characteristics and physiological changes during gestation, such as gestational weight gain (GWG), may have an influence in the overall burden of POPs in neonates. However, the associations between GWG and POP concentrations are still not well established.

Objective: We examined the association of GWG with cord serum POPs concentrations after adjusting for prepregnancy maternal body mass index (BMI) and other potential determinants of the transfer of POPs into newborns. The GWG values were evaluated after grouping by the reference guidelines of the Institute of Medicine (IOM).

Methods: We measured levels of 14 organochlorine pesticides, 7 polychlorobiphenyls (PCBs), and 14 polybrominated diphenyl ethers (PBDEs) in 325 cord serum samples from a Spanish birth cohort. Multivariable models were used to estimate associations of GWG, prepregnancy BMI, and other maternal determinants on cord serum concentrations of POPs.

Results: Neonatal concentrations of POPs were inversely associated with GWG after adjustment for age, prepregnancy BMI, educational level, and fish consumption. On average, neonates of women with IOM-recommended GWG have lower POP concentrations than do neonates of mothers with inadequate GWG.

Conclusions: The present findings suggest an association between neonatal exposure to POPs and inadequate GWG during pregnancy. Encouraging pregnant women to meet the recommended IOM guidelines for GWG may reduce the accumulation of POPs in newborns.

Exposure to Fine Particulate Matter during Pregnancy and Risk of Preterm Birth among Women in New Jersey, Ohio, and Pennsylvania, 2000–2005

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122:992–997 (September 2014)
<http://dx.doi.org/10.1289/ehp.1307456>

Background: Particulate matter ≤ 2.5 μm in aerodynamic diameter ($\text{PM}_{2.5}$) has been variably associated with preterm birth (PTB).

Objective: We classified PTB into four categories (20–27, 28–31, 32–34, and 35–36 weeks completed gestation) and estimated risk differences (RDs) for each category in association with a $1\text{-}\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ exposure during each week of gestation.

Methods: We assembled a cohort of singleton pregnancies that completed ≥ 20 weeks of gestation during 2000–2005 using live birth certificate data from three states (Pennsylvania, Ohio, and New Jersey) ($n = 1,940,213$; 8% PTB). We estimated mean $\text{PM}_{2.5}$ exposures for each week of gestation from monitor-corrected Community Multi-Scale Air Quality modeling data. RDs were estimated using modified Poisson linear regression and adjusted for maternal race/ethnicity, marital status, education, age, and ozone.

Results: RD estimates varied by exposure window and outcome period. Average $\text{PM}_{2.5}$ exposure during the fourth week of gestation was positively associated with all PTB outcomes, although magnitude varied by PTB category [e.g., for a $1\text{-}\mu\text{g}/\text{m}^3$ increase, $\text{RD} = 11.8$ (95% CI: $-6, 29.2$); $\text{RD} = 46$ (95% CI: $23.2, 68.9$); $\text{RD} = 61.1$ (95% CI: $22.6, 99.7$); and $\text{RD} = 28.5$ (95% CI: $-39, 95.7$) for preterm births during 20–27, 28–31, 32–34, and 35–36 weeks, respectively]. Exposures during the week of birth and the 2 weeks before birth also were positively associated with all PTB categories.

Conclusions: Exposures beginning around the time of implantation and near birth appeared to be more strongly associated with PTB than exposures during other time periods. Because particulate matter exposure is ubiquitous, evidence of effects of $\text{PM}_{2.5}$ exposure on PTB, even if small in magnitude, is cause for concern.

INFECTIONS

Associations between Extreme Precipitation and Gastrointestinal-Related Hospital Admissions in Chennai, India

Kathleen F. Bush, Marie S. O'Neill, Shi Li, Bhramar Mukherjee, Howard Hu, Santu Ghosh, and Kalpana Balakrishnan

122:249–254 (March 2014)
<http://dx.doi.org/10.1289/ehp.1306807>

Background: Understanding the potential links between extreme weather events and human health in India is important in the context of vulnerability and adaptation to climate change. Research exploring such linkages in India is sparse.

Objectives: We evaluated the association between extreme precipitation and gastrointestinal (GI) illness-related hospital admissions in Chennai, India, from 2004 to 2007.

Methods: Daily hospital admissions were extracted from two government hospitals in Chennai, India, and meteorological data were retrieved from the Chennai International Airport. We evaluated the association between extreme precipitation (≥ 90 th percentile) and hospital admissions using generalized additive models. Both single-day and distributed lag models were explored over a 15-day period, controlling for apparent temperature, day of week, and long-term time trends. We used a stratified analysis to explore the association across age and season.

Results: Extreme precipitation was consistently associated with GI-related hospital admissions. The cumulative summary of risk ratios estimated for a 15-day period corresponding to an extreme event (relative to no precipitation) was 1.60 (95% CI: 1.29, 1.98) among all ages, 2.72 (95% CI: 1.25, 5.92) among the young (≤ 5 years of age), and 1.62 (95% CI: 0.97, 2.70) among the old (≥ 65 years of age). The association was stronger during the pre-monsoon season (March–May), with a cumulative risk ratio of 6.50 (95% CI: 2.22, 19.04) for all ages combined compared with other seasons.

Conclusions: Hospital admissions related to GI illness were positively associated with extreme precipitation in Chennai, India, with positive cumulative risk ratios for a 15-day period following an extreme event in all age groups. Projected changes in precipitation and extreme weather events suggest that climate change will have important implications for human health in India, where health disparities already exist.

RELATED ARTICLE

NEWS | Rethinking Sterile: The Hospital Microbiome

Carrie Arnold | 122:A182 (July 2014)
<http://dx.doi.org/10.1289/ehp.122-A182>

Hospitals, despite the historical emphasis on sterility of health care environments, are now understood to be microbial ecosystems unto themselves. Investigators are studying these hospital microbiomes with an eye toward reducing hospital-acquired infections and optimizing patient health.



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FETAL OR EARLY-LIFE EXPOSURES CONTRIBUTING TO ADULT DISEASE

Serum Dioxin Concentrations and Bone Density and Structure in the Seveso Women's Health Study

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122:51–57 (January 2014)
<http://dx.doi.org/10.1289/ehp.1306788>

Background: 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD), a widespread environmental contaminant, is a known endocrine disruptor. In animal studies, TCDD exposure impairs bone metabolism and increases fragility. To our knowledge, no epidemiologic studies have examined this association.

Objectives: On 10 July 1976, a chemical explosion in Seveso, Italy, resulted in the highest known residential exposure to TCDD. In 1996, we initiated the Seveso Women's Health Study, a retrospective cohort study of the health of the women. In 2008, we followed up the cohort. Here, we evaluated the association between TCDD exposure and bone structure and geometry in adulthood, and considered whether timing of TCDD exposure before achievement of peak bone mass (assumed to occur 2 years after onset of menarche) modified the association.

Methods: Individual TCDD concentration was measured in archived serum collected soon after the explosion. In 2008, 350 women who were < 20 years old in 1976 underwent a dual-energy X-ray absorptiometry (DXA) bone scan. Bone mineral density was measured at the lumbar spine and hip, and hip geometry was extracted from hip DXA scans using the hip structural analysis method.

Results: Among premenopausal women, TCDD serum levels were associated with some indexes indicating better bone structure in women exposed before peak bone mass ($n = 219$), with stronger associations in those exposed before 5 years of age ($n = 46$). In contrast, among postmenopausal women, TCDD levels were associated with evidence of better bone structure in women exposed after peak bone mass ($n = 48$) than in other women ($n = 18$).

Conclusions: Our current results do not support the hypothesis that postnatal TCDD exposure adversely affects adult bone health. Continued follow-up of women who were youngest at exposure is warranted. Future studies should also focus on those exposed *in utero*.

Maternal Concentrations of Persistent Organochlorine Pollutants and the Risk of Asthma in Offspring: Results from a Prospective Cohort with 20 Years of Follow-up

Susanne Hansen, Marin Strøm, Sjurður F. Olsen, Ekaterina Maslova, Panu Rantakokko, Hannu Kiviranta, Dorte Rytter, Bodil H. Bech, Linda V. Hansen, and Thorhallur I. Halldorsson

122:93–99 (January 2014)
<http://dx.doi.org/10.1289/ehp.1206397>

Background: Previous findings suggest that developmental exposures to persistent organochlorine pollutants (POPs) may be detrimental for the development of the immune system in the offspring. Whether these suspected immunoregulatory effects persist beyond early childhood remains unclear.

Objectives: The objective of this study was to evaluate the association between maternal serum concentrations of POPs and the risk of asthma in offspring after 20 years of follow-up.

Methods: A birth cohort with 965 women was formed in 1988–1989 in Aarhus, Denmark. Concentrations of six polychlorinated biphenyls (PCBs) (congeners 118, 138, 153, 156, 170, 180), hexachlorobenzene (HCB), and dichlorodiphenyldichloroethylene (*p,p'*-DDE) were quantified in maternal serum ($n = 872$) collected in gestation week 30. Information about offspring use of asthma medications was obtained from the Danish Registry of Medicinal Product Statistics.

Results: Maternal serum concentrations of HCB and dioxin-like PCB-118 were positively associated with offspring asthma medication use after 20 years of follow-up (p for trend < 0.05). Compared with subjects in the first tertile of maternal concentration, those in the third tertile of PCB-118 had an adjusted hazard ratio (HR) of 1.90 (95% CI: 1.12, 3.23). For HCB the HR for the third versus the first tertile of maternal concentration was 1.92 (95% CI: 1.15, 3.21). Weak positive associations were also estimated for PCB-156 and the non-dioxin-like PCBs (PCBs 138, 153, 170, 180). No associations were found for *p,p'*-DDE.

Conclusions: Maternal concentrations of PCB-118 and HCB were associated with increased risk of asthma in offspring followed through 20 years of age.

» NEWS | SCIENCE SELECTION

A Long-Term Risk? Prenatal POPs Exposure and Asthma in Young Adults

Lindsey Konkel | 122:A28 (January 2014)
<http://dx.doi.org/10.1289/ehp.122-A28>

OBESITY

Urinary Polycyclic Aromatic Hydrocarbons and Childhood Obesity: NHANES (2001–2006)

Franco Scinicariello and Melanie C. Buser

122:299–303 (March 2014)

<http://dx.doi.org/10.1289/ehp.1307234>

Background: Polycyclic aromatic hydrocarbons (PAHs) are known carcinogens and suspected endocrine disruptors. Prenatal exposure to PAHs has been associated with obesity in early childhood.

Objective: We examined the association of urinary PAH metabolites with adiposity outcomes [body mass index (BMI) z-score, waist circumference (WC), and rate of obesity] in children and adolescents.

Methods: We performed whole-sample analyses of 3,189 individuals 6–19 years of age who participated in the 2001–2006 National Health and Nutrition Examination Survey. We performed multivariate linear and logistic regression to analyze the association of BMI z-score, WC, and obesity with concentrations of single urinary PAH compounds and the sum of PAHs. Furthermore, the analyses were stratified by developmental stage [i.e., children (6–11 years) and adolescents (12–19 years)].

Results: BMI z-score, WC, and obesity were positively associated with the molecular mass sum of the PAHs and the total sum of naphthalene metabolites. Most associations increased monotonically with increasing quartiles of exposure among children 6–11 years of age, whereas dose–response trends were less consistent for adolescents (12–19 years of age). Neither total PAHs nor total naphthalene metabolites were associated with overweight in either age group, and there was little evidence of associations between the outcomes and individual PAHs.

Conclusions: Total urinary PAH metabolites and naphthalene metabolites were associated with higher BMI, WC, and obesity in children 6–11 years of age, with positive but less consistent associations among adolescents.

Differences in BMI z-Scores between Offspring of Smoking and Nonsmoking Mothers: A Longitudinal Study of German Children from Birth through 14 Years of Age

Christina Riedel, Nora Fenske, Manfred J. Müller, Sandra Plachta-Danielzik, Thomas Keil, Linus Grabenhenrich, and Rüdiger von Kries

122:761–767 (July 2014)

<http://dx.doi.org/10.1289/ehp.1307139>

Background: Children of mothers who smoked during pregnancy have a lower birth weight but have a higher chance to become overweight during childhood.

Objectives: We followed children longitudinally to assess the age when higher body mass index (BMI) z-scores became evident in the children of mothers who smoked during pregnancy, and to evaluate the trajectory of changes until adolescence.

Methods: We pooled data from two German cohort studies that included repeated anthropometric measurements until 14 years of age and information on smoking during pregnancy and other risk factors for overweight. We used longitudinal quantile regression to estimate age- and sex-specific associations between maternal smoking and the 10th, 25th, 50th, 75th, and 90th quantiles of the BMI z-score distribution in study participants from birth through 14 years of age, adjusted for potential confounders. We used additive mixed models to estimate associations with mean BMI z-scores.

Results: Mean and median (50th quantile) BMI z-scores at birth were smaller in the children of mothers who smoked during pregnancy compared with children of nonsmoking mothers, but BMI z-scores were significantly associated with maternal smoking beginning at the age of 4–5 years, and differences increased over time. For example, the difference in the median BMI z-score between the daughters of smokers versus nonsmokers was 0.12 (95% CI: 0.01, 0.21) at 5 years, and 0.30 (95% CI: 0.08, 0.39) at 14 years of age. For lower BMI z-score quantiles, the association with smoking was more pronounced in girls, whereas in boys the association was more pronounced for higher BMI z-score quantiles.

Conclusions: A clear difference in BMI z-score (mean and median) between children of smoking and nonsmoking mothers emerged at 4–5 years of age. The shape and size of age-specific effect estimates for maternal smoking during pregnancy varied by age and sex across the BMI z-score distribution.

HEAVY METALS (E.G., LEAD, MERCURY)

Dietary Predictors of Maternal Prenatal Blood Mercury Levels in the ALSPAC Birth Cohort Study

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121:1214–1218 (October 2013)
<http://dx.doi.org/10.1289/ehp.1206115>

Background: Very high levels of prenatal maternal mercury have adverse effects on the developing fetal brain. It has been suggested that all possible sources of mercury should be avoided. However, although seafood is a known source of mercury, little is known about other dietary components that contribute to the overall levels of blood mercury.

Objective: Our goal was to quantify the contribution of components of maternal diet to prenatal blood mercury level.

Methods: Whole blood samples and information on diet and sociodemographic factors were collected from pregnant women ($n = 4,484$) enrolled in the Avon Longitudinal Study of Parents and Children (ALSPAC). The blood samples were assayed for total mercury using inductively coupled plasma dynamic reaction cell mass spectrometry. Linear regression was used to estimate the relative contributions of 103 dietary variables and 6 sociodemographic characteristics to whole blood total mercury levels (TBM; untransformed and log-transformed) based on R^2 values.

Results: We estimated that maternal diet accounted for 19.8% of the total variation in ln-TBM, with 44% of diet-associated variability (8.75% of the total variation) associated with seafood consumption (white fish, oily fish, and shellfish). Other dietary components positively associated with TBM included wine and herbal teas, and components with significant negative associations included white bread, meat pies or pasties, and french fries.

Conclusions: Although seafood is a source of dietary mercury, seafood appeared to explain a relatively small proportion of the variation in TBM in our UK study population. Our findings require confirmation, but suggest that limiting seafood intake during pregnancy may have a limited impact on prenatal blood mercury levels.

Maternal Blood, Plasma, and Breast Milk Lead: Lactational Transfer and Contribution to Infant Exposure

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122:87–92 (January 2014)
<http://dx.doi.org/10.1289/ehp.1307187>

Background: Human milk is a potential source of lead exposure. Yet lactational transfer of lead from maternal blood into breast milk and its contribution to infant lead burden remains poorly understood.

Objectives: We explored the dose–response relationships between maternal blood, plasma, and breast milk to better understand lactational transfer of lead from blood and plasma into milk and, ultimately, to the breastfeeding infant.

Methods: We measured lead in 81 maternal blood, plasma, and breast milk samples at 1 month postpartum and in 60 infant blood samples at 3 months of age. Milk-to-plasma (M/P) lead ratios were calculated. Multivariate linear, piecewise, and generalized additive models were used to examine dose–response relationships between blood, plasma, and milk lead levels.

Results: Maternal lead levels (mean \pm SD) were as follows: blood: 7.7 ± 4.0 $\mu\text{g}/\text{dL}$; plasma: 0.1 ± 0.1 $\mu\text{g}/\text{L}$; milk: 0.8 ± 0.7 $\mu\text{g}/\text{L}$. The average M/P lead ratio was 7.7 (range, 0.6–39.8) with 97% of the ratios being > 1 . The dose–response relationship between plasma lead and M/P ratio was nonlinear (empirical distribution function = 6.5, $p = 0.0006$) with the M/P ratio decreasing by 16.6 and 0.6 per 0.1 $\mu\text{g}/\text{L}$ of plasma lead, respectively, below and above 0.1 $\mu\text{g}/\text{L}$ plasma lead. Infant blood lead level (3.4 ± 2.2 $\mu\text{g}/\text{dL}$) increased by 1.8 $\mu\text{g}/\text{dL}$ per 1 $\mu\text{g}/\text{L}$ milk lead ($p < 0.0001$, $R^2 = 0.3$).

Conclusions: The M/P ratio for lead in humans is substantially higher than previously reported, and transfer of lead from plasma to milk may be higher at lower levels of plasma lead. Breast milk is an important determinant of lead burden among breastfeeding infants.

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Lead Transfer during Breastfeeding: A Start toward Filling in the Data Gaps

Julia R. Barrett | 122:A26 (January 2014)
<http://dx.doi.org/10.1289/ehp.122-A26>

Mercury Exposure and Health Impacts among Individuals in the Artisanal and Small-Scale Gold Mining Community: A Comprehensive Review

Herman Gibb and Keri Grace O'Leary

122:667–672 (July 2014)

<http://dx.doi.org/10.1289/ehp.1307864>

Background: Mercury (Hg) is used in gold mining to extract gold from ore by forming “amalgam”—a mixture composed of approximately equal parts mercury and gold. Approximately 15 million people, including approximately 3 million women and children, participate in artisanal small-scale gold mining (ASGM) in developing countries. Thirty-seven percent of global air emissions of Hg are produced by ASGM. The recently adopted Minamata Convention calls for nations to gather health data, train health-care workers, and raise awareness in regard to ASGM activity.

Objective: The purpose of our review was to evaluate the current literature regarding the health effects of Hg among those working and/or living in or near ASGM communities.

Methods: We searched PubMed, ScienceDirect, and Google Scholar for studies relating to health effects and biomarkers of Hg exposure in ASGM communities. Articles published from 1990 through December 2012 were evaluated for relevance.

Discussion: Studies reporting health assessments, kidney dysfunction, neurological disorders and symptoms, and immunotoxicity/autoimmune dysfunction in individuals living in or near an ASGM community were identified. More than 60 studies that measured biomarkers of Hg exposure in individuals living in or near ASGM communities were also identified. These studies, conducted in 19 different countries in South America, Asia, and Africa, demonstrated that hair and urine concentrations are well above World Health Organization health guidance values in ASGM communities.

Conclusions: ASGM workers and their families are exposed to Hg vapor, and workers, workers' families, and residents of nearby and downstream communities are consuming fish heavily contaminated with methylmercury.

RELATED ARTICLES

NEWS | Lead-Based Decorative Paints: Where Are They Still Sold—and Why?

Rebecca Kessler | 122:A96 (April 2014)
<http://dx.doi.org/10.1289/ehp.122-A96>

Decades ago developed nations began banning lead-based paint for residential use, yet few developing countries regulate lead in paint at all. And decorative paints with high lead content are readily available on store shelves in these countries, rarely bearing any labeling to warn consumers of the dangers they pose, according to a spate of recent studies. Now, however, an international effort is gathering steam to remove lead from decorative paints once and for all.

NEWS | Low-Dose Arsenic: In Search of a Risk Threshold

Charles W. Schmidt | 122:A130 (May 2014)
<http://dx.doi.org/10.1289/ehp.122-A130>

Exposure to harmful levels of arsenic may be more widespread than previously recognized. Protecting against low-level exposure is challenging, however, given arsenic's ubiquity. Moreover, disagreement over the evidence for low-dose effects poses a problem for regulators who face mounting pressure to set or reduce standards for arsenic.

NEWS | The Minamata Convention on Mercury: A First Step toward Protecting Future Generations

Rebecca Kessler | 121:A304 (October 2013)
<http://dx.doi.org/10.1289/ehp.121-A304>

The Minamata disaster was the first large-scale incident of methylmercury poisoning, and it drew the world's attention to the devastating effects of this powerful neurotoxicant, now known to be particularly dangerous to fetuses, infants, and young children. In October 2013 a new convention to control mercury emissions opens for signing in Japan in recognition of the fact that mercury pollution is a global problem no one country can solve alone.



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EDITORIAL | Childhood Lead Poisoning in China: Challenges and Opportunities

Chong-huai Yan, Jian Xu, and Xiao-ming Shen | 121:A294 (October 2013)
<http://dx.doi.org/10.1289/ehp.1307558>

The Influence of Declining Air Lead Levels on Blood Lead–Air Lead Slope Factors in Children

Jennifer Richmond-Bryant, Qingyu Meng, Allen Davis, Jonathan Cohen, Shou-En Lu, David Svendsgaard, James S. Brown, Lauren Tuttle, Heidi Hubbard, Joann Rice, Ellen Kirrane, Lisa C. Vinikoor-Imler, Dennis Kotchmar, Erin P. Hines, and Mary Ross

122:754–760 (July 2014)
<http://dx.doi.org/10.1289/ehp.1307072>

Background: It is difficult to discern the proportion of blood lead (PbB) attributable to ambient air lead (PbA), given the multitude of lead (Pb) sources and pathways of exposure. The PbB–PbA relationship has previously been evaluated across populations. This relationship was a central consideration in the 2008 review of the Pb national ambient air quality standards.

Objectives: The objectives of this study were to evaluate the relationship between PbB and PbA concentrations among children nationwide for recent years and to compare the relationship with those obtained from other studies in the literature.

Methods: We merged participant-level data for PbB from the National Health and Nutrition Examination Survey (NHANES) III (1988–1994) and NHANES 9908 (1999–2008) with PbA data from the U.S. Environmental Protection Agency. We applied mixed-effects models, and we computed slope factor, $d[PbB]/d[PbA]$ or the change in PbB per unit change in PbA, from the model results to assess the relationship between PbB and PbA.

Results: Comparing the NHANES regression results with those from the literature shows that slope factor increased with decreasing PbA among children 0–11 years of age.

Conclusion: These findings suggest that a larger relative public health benefit may be derived among children from decreases in PbA at low PbA exposures. Simultaneous declines in Pb from other sources, changes in PbA sampling uncertainties over time largely related to changes in the size distribution of Pb-bearing particulate matter, and limitations regarding sampling size and exposure error may contribute to the variability in slope factor observed across peer-reviewed studies.

PESTICIDES AND OTHER CHEMICALS/COMPOUNDS (E.G., BPA, PCBS, PBDES, PFCS, PHTHALATES, ENDOCRINE DISRUPTORS)

Phthalate Exposure and Allergy in the U.S. Population: Results from NHANES 2005–2006

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121:1129–1134 (October 2013)
<http://dx.doi.org/10.1289/ehp.1206211>

Background: Environmental exposures to phthalates, particularly high-molecular-weight (HMW) phthalates, are suspected to contribute to allergy.

Objective: We assessed whether phthalate metabolites are associated with allergic symptoms and sensitization in a large nationally representative sample.

Methods: We used data on urinary phthalate metabolites and allergic symptoms (hay fever, rhinitis, allergy, wheeze, asthma) and sensitization from participants ≥ 6 years of age in the National Health and Nutrition Examination Survey (NHANES) 2005–2006. Allergen sensitization was defined as a positive response to at least one of 19 specific IgE antigens (≥ 0.35 kU/L). Odds ratios (ORs) per one \log_{10} unit change in phthalate concentration were estimated using logistic regression adjusting for age, race, body mass index, gender, creatinine, and cotinine. Separate analyses were conducted for children (6–17 years of age) and adults.

Results: The HMW phthalate metabolite monobenzyl phthalate (MBzP) was the only metabolite positively associated with current allergic symptoms in adults (wheeze, asthma, hay fever, and rhinitis). Mono-(3-carboxypropyl) phthalate and the sum of diethylhexyl phthalate metabolites (both representing HMW phthalate exposures) were positively associated with allergic sensitization in adults. Conversely, in children, HMW phthalate metabolites were inversely associated with asthma and hay fever. Of the low-molecular-weight phthalate metabolites, monoethyl phthalate was inversely associated with allergic sensitization in adults (OR = 0.79; 95% CI: 0.70, 0.90).

Conclusion: In this cross-sectional analysis of a nationally representative sample, HMW phthalate metabolites, particularly MBzP, were positively associated with allergic symptoms and sensitization in adults, but there was no strong evidence for associations between phthalates and allergy in children 6–17 years of age.

Prenatal Exposure to Environmental Phenols: Concentrations in Amniotic Fluid and Variability in Urinary Concentrations during Pregnancy

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121:1225–1231 (October 2013)
<http://dx.doi.org/10.1289/ehp.1206335>

Background: Maternal urinary biomarkers are often used to assess fetal exposure to phenols and their precursors. Their effectiveness as a measure of exposure in epidemiological studies depends on their variability during pregnancy and their ability to accurately predict fetal exposure.

Objectives: We assessed the relationship between urinary and amniotic fluid concentrations of nine environmental phenols, and the reproducibility of urinary concentrations, among pregnant women.

Methods: Seventy-one women referred for amniocentesis were included. Maternal urine was collected at the time of the amniocentesis appointment and on two subsequent occasions. Urine and amniotic fluid were analyzed for 2,4- and 2,5-dichlorophenols, bisphenol A, benzophenone-3, triclosan, and methyl-, ethyl-, propyl-, and butylparabens using online solid phase extraction–high performance liquid chromatography–isotope dilution tandem mass spectrometry.

Results: Only benzophenone-3 and propylparaben were detectable in more than half of the amniotic fluid samples; for these phenols, concentrations in amniotic fluid and maternal urine collected on the same day were positively correlated ($\rho = 0.53$ and 0.32 , respectively). Other phenols were detected infrequently in amniotic fluid (e.g., bisphenol A was detected in only two samples). The intraclass correlation coefficients (ICCs) of urinary concentrations in samples from individual women ranged from 0.48 to 0.62 for all phenols except bisphenol A (ICC = 0.11).

Conclusion: Amniotic fluid detection frequencies for most phenols were low. The reproducibility of urine measures was poor for bisphenol A, but good for the other phenols. Although a single sample may provide a reasonable estimate of exposure for some phenols, collecting multiple urine samples during pregnancy is an option to reduce exposure measurement error in studies regarding the effects of phenol prenatal exposure on health.

Predictors of Serum Chlorinated Pesticide Concentrations among Prepubertal Russian Boys

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121:1372–1377 (November–December 2013)
<http://dx.doi.org/10.1289/ehp.1306480>

Background: Few studies have evaluated predictors of childhood exposure to organochlorine pesticides (OCPs), a class of lipophilic persistent chemicals.

Objectives: Our goal was to identify predictors of serum OCP concentrations—hexachlorobenzene (HCB), β -hexachlorocyclohexane (β -HCH), and p,p' -dichlorodiphenyldichloroethylene (p,p' -DDE)—among boys in Chapaevsk, Russia.

Methods: Between 2003 and 2005, 499 boys 8–9 years of age were recruited in a prospective cohort. The initial study visit included a physical examination; blood collection; health, lifestyle, and food-frequency questionnaires; and determination of residential distance from a local factory complex that produced HCB and β -HCH. Fasting serum samples were analyzed for OCPs at the U.S. Centers for Disease Control and Prevention. General linear regression models were used to identify predictors of the boys' serum HCB, β -HCH, and p,p' -DDE concentrations.

Results: Among 355 boys with OCP measurements, median serum HCB, β -HCH, and p,p' -DDE concentrations were 158, 167, and 284 ng/g lipid, respectively. Lower body mass index, longer breastfeeding duration, and local dairy consumption were associated with higher concentrations of OCPs. Boys who lived < 2 km from the factory complex had 64% (95% CI: 37, 96) and 57% (95% CI: 32, 87) higher mean HCB and β -HCH concentrations, respectively, than boys who lived ≥ 5 km away. Living > 3 years in Chapaevsk predicted higher β -HCH concentrations, and having parents who lacked a high school education predicted higher p,p' -DDE concentrations.

Conclusions: Among this cohort of prepubertal Russian boys, predictors of serum OCPs included consumption of local dairy products, longer local residence, and residential proximity to the local factory complex.

Urinary Metabolites of Organophosphate and Pyrethroid Pesticides and Behavioral Problems in Canadian Children

Youssef Oulhote and Maryse F. Bouchard

121:1378–1384 (November–December 2013)

<http://dx.doi.org/10.1289/ehp.1306667>

Background: Exposure to organophosphate pesticides has been associated with neurobehavioral deficits in children, although data on low levels of exposure experienced by the general population are sparse. Pyrethroids are insecticides rapidly gaining popularity, and epidemiological evidence on their potential effects is lacking.

Objective: We examined the association between exposure to organophosphate and pyrethroid pesticides, indicated by urinary metabolites, and parentally reported behavioral problems in children.

Methods: We used data on children 6–11 years of age from the Canadian Health Measures Survey (2007–2009). We used logistic regressions to estimate odds ratios (ORs) for high scores on the Strengths and Difficulties Questionnaire (SDQ), which may indicate behavioral problems, in association with concentrations of pyrethroid and organophosphate metabolites in the urine of 779 children, adjusting for covariates (sex, age, race/ethnicity, income, parental education, blood lead levels, maternal smoking during pregnancy, and others).

Results: At least one urinary metabolite for organophosphates was detected in 91% of children, and for pyrethroids in 97% of children. Organophosphate metabolites were not significantly associated with high SDQ scores. The pyrethroid metabolite *cis*-DCCA [3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid] was significantly associated with high scores for total difficulties on the SDQ (OR for a 10-fold increase = 2.0; 95% CI: 1.1, 3.6), and there was a nonsignificant association with *trans*-DCCA (OR = 1.6; 95% CI: 0.9, 3.0).

Conclusion: In contrast with previous studies, we did not observe an association between exposure to organophosphate pesticides and behavioral scores in children. However, some pyrethroid urinary metabolites were associated with a high level of parent-reported behavioral problems. Longitudinal studies should be conducted on the potential risks of pyrethroids.

Evaluation of Polycyclic Aromatic Hydrocarbons Using Analytical Methods, Toxicology, and Risk Assessment Research: Seafood Safety after a Petroleum Spill as an Example

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122:6–9 (January 2014)

<http://dx.doi.org/10.1289/ehp.1306724>

Background: Polycyclic aromatic hydrocarbons (PAHs) are abundant and widespread environmental chemicals. They are produced naturally and through man-made processes, and they are common in organic media, including petroleum. Several PAHs are toxic, and a subset exhibit carcinogenic activity. PAHs represent a range of chemical structures based on two or more benzene rings and, depending on their source, can exhibit a variety of side modifications resulting from oxygenation, nitrogenation, and alkylation.

Objectives: Here we discuss the increasing ability of contemporary analytical methods to distinguish not only different chemical structures among PAHs but also their concentrations in environmental media. Using seafood contamination following the *Deepwater Horizon* accident as an example, we identify issues that are emerging in the PAH risk assessment process because of increasing analytical sensitivity for individual PAHs, and we describe the paucity of toxicological literature for many of these compounds.

Discussion: PAHs, including the large variety of chemically modified or substituted PAHs, are naturally occurring and may constitute health risks if human populations are exposed to hazardous levels. However, toxicity evaluations have not kept pace with modern analytic methods and their increased ability to detect substituted PAHs. Therefore, although it is possible to measure these compounds in seafood and other media, we do not have sufficient information on the potential toxicity of these compounds to incorporate them into human health risk assessments and characterizations.

Conclusions: Future research efforts should strategically attempt to fill this toxicological knowledge gap so human health risk assessments of PAHs in environmental media or food can be better determined. This is especially important in the aftermath of petroleum spills.

Exposure to Brominated Trihalomethanes in Water During Pregnancy and Micronuclei Frequency in Maternal and Cord Blood Lymphocytes

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122:100–106 (January 2014)
<http://dx.doi.org/10.1289/ehp.1206434>

Background: Water disinfection by-products have been associated with an increased cancer risk. Micronuclei (MN) frequency in lymphocytes is a marker of genomic damage and can predict adult cancer risk.

Objective: We evaluated maternal exposure to drinking water brominated trihalomethanes (BTHM) in relation to MN frequency in maternal and cord blood lymphocytes.

Methods: MN frequency was examined in 214 mothers and 223 newborns from the Rhea mother–child cohort in Crete, Greece, in 2007–2008. Residential BTHM water concentrations were estimated during pregnancy using tap water analyses and modeling. Questionnaires on water related habits were used to estimate BTHM exposure from all routes. Associations between BTHM and MN frequency were estimated using negative binomial regression.

Results: BTHM concentrations in residential tap water during pregnancy ranged from 0.06 to 7.1 µg/L. MN frequency in maternal binucleated lymphocytes was found to increase with BTHM concentrations in residential water for exposure during the first [rate ratio (RR) for 1 µg/L = 1.05; 95% CI: 1.00, 1.11] and second trimesters (RR for 1 µg/L = 1.03; 95% CI: 1.00, 1.06), and through all routes of BTHM exposure during the first trimester (RR for 1 µg/week = 3.14; 95% CI: 1.16, 8.50).

Conclusions: These findings suggest that exposure to BTHM may increase the frequency of MN in maternal binucleated lymphocytes.

Evaluating the Effectiveness of Fish Consumption Advisories: Modeling Prenatal, Postnatal, and Childhood Exposures to Persistent Organic Pollutants

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122:178–186 (February 2014)
<http://dx.doi.org/10.1289/ehp.1206380>

Background: Because human exposure to persistent organic pollutants (POPs) occurs mainly through ingestion of contaminated food, regulatory bodies issue dietary consumption advisories to describe safe intake levels for food items of concern, particularly fish.

Objectives: Our study goal was to estimate the effectiveness of fish consumption advisories in reducing exposure of infants and children to POPs.

Methods: We used the time-variant mechanistic model CoZMoMAN to estimate and compare prenatal, postnatal, and childhood exposure to polychlorinated biphenyl congener PCB-153 under different scenarios of maternal guideline adherence for both hypothetical constant and realistic time-variant chemical emissions. The scenarios differed in terms of length of compliance (1 vs. 5 years), extent of fish substitution (all vs. half), and replacement diet (uncontaminated produce vs. beef). We also estimated potential exposure reductions for a range of theoretical chemicals to explore how guideline effectiveness varies with a chemical's partitioning and degradation properties.

Results: When assuming realistic time periods of advisory compliance, our findings suggest that temporarily eliminating or reducing maternal fish consumption is largely ineffective in reducing pre- and postnatal exposure to substances with long elimination half-lives in humans, especially during periods of decreasing environmental emissions. Substituting fish with beef may actually result in higher exposure to certain groups of environmental contaminants. On the other hand, advisories may be highly effective in reducing exposure to substances with elimination half-lives in humans shorter than the length of compliance.

Conclusions: Our model estimates suggest that fish consumption advisories are unlikely to be effective in reducing prenatal, postnatal, and childhood exposures to compounds with long elimination half-lives in humans.

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Fish Consumption Caveat: Advisories May Not Help with Long-Lived Contaminants

Kellyn S. Betts | 122:A57 (February 2014)
<http://dx.doi.org/10.1289/ehp.122-A57>

Breastfeeding: A Potential Excretion Route for Mothers and Implications for Infant Exposure to Perfluoroalkyl Acids

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122:187–192 (February 2014)
<http://dx.doi.org/10.1289/ehp.1306613>

Background: The presence of perfluoroalkyl acids (PFAAs) in breast milk has been documented, but their lactational transfer has been rarely studied. Determination of the elimination rates of these chemicals during breastfeeding is important and critical for assessing exposure in mothers and infants.

Objectives: We aimed to investigate the association between breastfeeding and maternal serum concentrations of perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorononanoic acid (PFNA), and perfluorohexane sulfonate (PFHxS). For a subset of the population, for whom we also have their infants' measurements, we investigated associations of breastfeeding with infant serum PFAA concentrations.

Methods: The present analysis included 633 women from the C8 Science Panel Study who had a child < 3.5 years of age and who provided blood samples and reported detailed information on breastfeeding at the time of survey. PFAA serum concentrations were available for all mothers and 8% ($n = 49$) of the infants. Maternal and infant serum concentrations were regressed on duration of breastfeeding.

Results: Each month of breastfeeding was associated with lower maternal serum concentrations of PFOA (–3%; 95% CI: –5, –2%), PFOS (–3%; 95% CI: –3, –2%), PFNA (–2%; 95% CI: –2, –1%), and PFHxS (–1%; 95% CI: –2, 0%). The infant PFOA and PFOS serum concentrations were 6% (95% CI: 1, 10%) and 4% (95% CI: 1, 7%) higher per month of breastfeeding.

Conclusions: Breast milk is the optimal food for infants, but is also a PFAA excretion route for lactating mothers and exposure route for nursing infants.

Within- and Between-Child Variation in Repeated Urinary Pesticide Metabolite Measurements over a 1-Year Period

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122:201–206 (February 2014)
<http://dx.doi.org/10.1289/ehp.1306737>

Background: Children are exposed to pesticides from many sources and routes, including dietary and incidental ingestion, dermal absorption, and inhalation. Linking health outcomes to these exposures using urinary metabolites requires understanding temporal variability within subjects to avoid exposure misclassification.

Objectives: We characterized the within- and between-child variability of urinary organophosphorus and pyrethroid metabolites in 23 participants of the Children's Pesticide Exposure Study–Washington over 1 year and examined the ability of one to four spot urine samples to categorize mean exposures.

Methods: Each child provided urine samples twice daily over 7- to 16-day sessions in four seasons in 2003 and 2004. Samples were analyzed for five pyrethroid and five organophosphorus (OP) metabolites. After adjusting for specific gravity, we used a customized maximum likelihood estimation linear mixed-effects model that accounted for values below the limit of detection to calculate intraclass correlation coefficients (ICC) and conducted surrogate category analyses.

Results: Within-child variability was 2–11 times greater than between-child variability. When restricted to samples collected during a single season, ICCs were higher in the fall, winter, and spring than in summer for OPs, and higher in summer and winter for pyrethroids, indicating an increase in between-person variability relative to within-person variability during these seasons. Surrogate category analyses demonstrated that a single spot urine sample did not categorize metabolite concentrations well, and that four or more samples would be needed to categorize children into quartiles consistently.

Conclusions: Urinary biomarkers of these short half-life pesticides exhibited substantial within-person variability in children observed over four seasons. Researchers investigating pesticides and health outcomes in children may need repeated biomarker measurements to derive accurate estimates of exposure and relative risks.

Temporal Trends in Phthalate Exposures: Findings from the National Health and Nutrition Examination Survey, 2001–2010

Ami R. Zota, Antonia M. Calafat, and Tracey J. Woodruff

122:235–241 (March 2014)

<http://dx.doi.org/10.1289/ehp.1306681>

Background: Phthalates are ubiquitous environmental contaminants. Because of potential adverse effects on human health, butylbenzyl phthalate [BBzP; metabolite, monobenzyl phthalate (MBzP)], di-*n*-butyl phthalate [DnBP; metabolite, mono-*n*-butyl phthalate (MnBP)], and di(2-ethylhexyl) phthalate (DEHP) are being replaced by substitutes including other phthalates; however, little is known about consequent trends in population-level exposures.

Objective: We examined temporal trends in urinary concentrations of phthalate metabolites in the general U.S. population and whether trends vary by sociodemographic characteristics.

Methods: We combined data on 11 phthalate metabolites for 11,071 participants from five cycles of the National Health and Nutrition Examination Survey (2001–2010). Percent changes and least square geometric means (LSGMs) were calculated from multivariate regression models.

Results: LSGM concentrations of monoethyl phthalate, MnBP, MBzP, and Σ DEHP metabolites decreased between 2001–2002 and 2009–2010 [percent change (95% CI): –42% (–49, –34); –17% (–23, –9); –32% (–39, –23) and –37% (–46, –26), respectively]. In contrast, LSGM concentrations of monoisobutyl phthalate, mono(3-carboxypropyl) phthalate (MCPP), monocarboxyoctyl phthalate, and monocarboxynonyl phthalate (MCNP) increased over the study period [percent change (95% CI): 206% (178, 236); 25% (8, 45); 149% (102, 207); and 15% (1, 30), respectively]. Trends varied by subpopulations for certain phthalates. For example, LSGM concentrations of Σ DEHP metabolites, MCPP, and MCNP were higher in children than adults, but the gap between groups narrowed over time ($p_{\text{interaction}} < 0.01$).

Conclusions: Exposure of the U.S. population to phthalates has changed in the last decade. Data gaps make it difficult to explain trends, but legislative activity and advocacy campaigns by nongovernmental organizations may play a role in changing trends.

Behavioral Sexual Dimorphism in School-Age Children and Early Developmental Exposure to Dioxins and PCBs: A Follow-Up Study of the Duisburg Cohort

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122:292–298 (March 2014)

<http://dx.doi.org/10.1289/ehp.1306533>

Background: Polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) and polychlorinated biphenyls (PCBs) are persistent organic pollutants that have been characterized as endocrine-disrupting chemicals (EDCs).

Objectives: Within the Duisburg birth cohort study, we studied associations of prenatal exposure to PCDD/Fs and PCBs with parent-reported sexually dimorphic behavior in children.

Methods: We measured lipid-based and WHO₂₀₀₅-TEQ (toxic equivalents established in 2005 by the World Health Organization)—standardized PCDD/Fs and PCBs in maternal blood samples and in early breast milk using gas chromatography/high-resolution mass spectrometry. At the child's age of 6–8 years, parents (mostly mothers) reported sex-typical characteristics, preferred toys, and play activities using the Pre-School Activities Inventory (PSAI), which was used to derive feminine, masculine, and difference (feminine – masculine) scores. We estimated exposure–outcome associations using multivariate linear regression. A total of 91–109 children were included in this follow-up.

Results: Mean blood levels of summed WHO₂₀₀₅-TEQ-standardized dioxins (Σ PCDD/Fs) were 14.5 ± 6.4 pg/g blood lipids, and Σ PCBs were 6.9 ± 3.8 pg/g blood lipids, with similar values for milk lipids. Regression analyses revealed some highly significant interactions between sex and exposure—such as for Σ PCBs in milk, pronounced positive (boys: $\beta = 3.24$; CI = 1.35, 5.14) or negative (girls: $\beta = -3.59$; CI = –1.10, –6.08) associations with reported femininity. Less pronounced and mostly insignificant but consistent associations were found for the masculinity score, positive for boys and negative for girls.

Conclusions: Given our results and the findings of previous studies, we conclude that there is sufficient evidence that these EDCs modify behavioral sexual dimorphism in children, presumably by interacting with the hypothalamic–pituitary–gonadal axis.

Relationships of Polychlorinated Biphenyls and Dichlorodiphenyldichloroethylene (*p,p'*-DDE) with Testosterone Levels in Adolescent Males

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122:304–309 (March 2014)
<http://dx.doi.org/10.1289/ehp.1205984>

Background: Concern persists over endocrine-disrupting effects of persistent organic pollutants (POPs) on human growth and sexual maturation. Potential effects of toxicant exposures on testosterone levels during puberty are not well characterized.

Objectives: In this study we evaluated the relationship between toxicants [polychlorinated biphenyls (PCBs), dichlorodiphenyldichloroethylene (*p,p'*-DDE), hexachlorobenzene (HCB), and lead] and testosterone levels among 127 Akwesasne Mohawk males 10 to < 17 years of age with documented toxicant exposures.

Methods: Data were collected between February 1996 and January 2000. Fasting blood specimens were collected before breakfast by trained Akwesasne Mohawk staff. Multivariable regression models were used to estimate associations between toxicants and serum testosterone, adjusted for other toxicants, Tanner stage, and potential confounders.

Results: The sum of 16 PCB congeners ($\Sigma 16\text{PCBs}$) that were detected in $\geq 50\%$ of the population was significantly and negatively associated with serum testosterone levels, such that a 10% change in exposure was associated with a 5.6% decrease in testosterone (95% CI: -10.8 , -0.5%). Of the 16 congeners, the more persistent ones ($\Sigma 8\text{PerPCBs}$) were related to testosterone, whereas the less persistent ones, possibly reflecting more recent exposure, were not. When PCB congeners were subgrouped, the association was significant for the sum of eight more persistent PCBs (5.7% decrease; 95% CI: -11 , -0.4%), and stronger than the sum of six less persistent congeners (3.1% decrease; 95% CI: -7.2 , 0.9%). *p,p'*-DDE was positively but not significantly associated with serum testosterone (5.2% increase with a 10% increase in exposure; 95% CI: -0.5 , 10.9%). Neither lead nor HCB was significantly associated with testosterone levels.

Conclusions: Exposure to PCBs, particularly the more highly persistent congeners, may negatively influence testosterone levels among adolescent males. The positive relationship between *p,p'*-DDE and testosterone indicates that not all POPs act similarly.

Urinary Concentrations of 2,4-Dichlorophenol and 2,5-Dichlorophenol in the U.S. Population (National Health and Nutrition Examination Survey, 2003–2010): Trends and Predictors

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122:351–355 (April 2014)
<http://dx.doi.org/10.1289/ehp.1306816>

Background: 2,4-Dichlorophenol (2,4-DCP), 2,5-dichlorophenol (2,5-DCP), and their precursors are widely used in industry and in consumer products. Urinary concentrations of these dichlorophenols (DCPs) have been measured as part of four National Health and Nutrition Examination Survey (NHANES) cycles in order to assess the exposure to these compounds or their precursors among the general U.S. population.

Objectives: We identified predictors and evaluated trends in DCP concentrations according to race/ethnicity, age, sex, family income, and housing type.

Methods: We used analysis of covariance to examine associations of various demographic parameters and survey cycle with urinary concentrations of DCPs during NHANES 2003–2010. We also conducted weighted logistic regressions to estimate associations of DCP concentrations above the 95th percentile with housing type, race/ethnicity, and income.

Results: We detected DCPs in at least 81% of participants. Geometric mean (GM) urinary concentrations were higher for 2,5-DCP ($6.1\text{--}12.9\text{ }\mu\text{g/L}$) than 2,4-DCP ($0.8\text{--}1.0\text{ }\mu\text{g/L}$) throughout 2003–2010. Adjusted GM concentrations of the DCPs among children (6–11 years of age) and adults > 60 years of age were higher than among adolescents and other adults. Adjusted GM concentrations among non-Hispanic whites were lower than among non-Hispanic blacks and Mexican Americans, although differences according to race/ethnicity were less pronounced among participants in high-income households. Among non-Hispanic blacks and Mexican Americans, adjusted GM concentrations were lowest among high-income participants relative to other income groups, with a monotonic decrease with increasing income among Mexican Americans. Type of housing and race/ethnicity were significant predictors of DCP urinary concentrations above the 95th percentile. Furthermore, urinary DCP concentrations have showed a downward trend since 2003.

Conclusions: Exposure to DCPs and their precursors was prevalent in the general U.S. population in 2003–2010. We identified age and race/ethnicity, family income, and housing type as predictors of exposure to these compounds.

Association between Maternal Serum Perfluoroalkyl Substances during Pregnancy and Maternal and Cord Thyroid Hormones: Taiwan Maternal and Infant Cohort Study

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122:529–534 (May 2014)
<http://dx.doi.org/10.1289/ehp.1306925>

Background: Perfluoroalkyl substances (PFASs) are synthetic compounds that are widely used in industry and are often detectable in humans. In pregnant rats and their pups, PFASs can interfere with thyroid hormone homeostasis. In humans, maternal thyroid hormones supply the fetus throughout pregnancy, and thyroid hormones play a critical role in fetal growth and neurodevelopment.

Objectives: We investigated the association between maternal PFAS exposure and thyroid hormone status in pregnant women and neonates.

Methods: In a study of environmental exposure and health in Taiwan, we measured serum concentrations of nine PFASs and four thyroid hormones for 285 pregnant women in their third trimester, and also measured cord serum thyroid hormones for 116 neonates. Associations between maternal PFASs and maternal and cord thyroid hormones were examined in multiple linear regression models.

Results: Perfluorohexanesulfonic acid concentrations were positively associated with maternal thyroid-stimulating hormone (TSH) levels. Pregnant women with higher levels of perfluorononanoic acid (PFNA), perfluoroundecanoic acid (PFUnDA), and perfluorododecanoic acid (PFDoDA) had lower free thyroxine (T_4) and total T_4 levels. For example, we estimated that maternal free T_4 levels decreased 0.019 ng/dL (95% CI: –0.028, –0.009) with each nanogram per milliliter increase in maternal PFNA. Finally, maternal PFNA, PFUnDA, and PFDoDA levels were associated with lower cord total triiodothyronine (T_3) and total T_4 levels, and maternal perfluorodecanoic acid (PFDeA) was associated with lower cord total T_3 .

Conclusions: Our results suggest that exposure to some PFASs during pregnancy may interfere with thyroid hormone homeostasis in pregnant women and fetuses.

Predictors of Blood Trihalomethane Concentrations in NHANES 1999–2006

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122:695–702 (July 2014)
<http://dx.doi.org/10.1289/ehp.1306499>

Background: Trihalomethanes (THMs) are water disinfection by-products that have been associated with bladder cancer and adverse birth outcomes. Four THMs (bromoform, chloroform, bromodichloromethane, dibromochloromethane) were measured in blood and tap water of U.S. adults in the National Health and Nutrition Examination Survey (NHANES) 1999–2006. THMs are metabolized to potentially toxic/mutagenic intermediates by cytochrome p450 (CYP) 2D6 and CYP2E1 enzymes.

Objectives: We conducted exploratory analyses of blood THMs, including factors affecting CYP2D6 and CYP2E1 activity.

Methods: We used weighted multivariable regressions to evaluate associations between blood THMs and water concentrations, survey year, and other factors potentially affecting THM exposure or metabolism (e.g., prescription medications, cruciferous vegetables, diabetes, fasting, pregnancy, swimming).

Results: From 1999 to 2006, geometric mean blood and water THM levels dropped in parallel, with decreases of 32%–76% in blood and 38%–52% in water, likely resulting, in part, from the lowering of the total THM drinking water standard in 2002–2004. The strongest predictors of blood THM levels were survey year and water concentration ($n = 4,232$ total THM; $n = 4,080$ bromoform; $n = 4,582$ chloroform; $n = 4,374$ bromodichloromethane; $n = 4,464$ dibromochloromethane). We detected statistically significant inverse associations with diabetes and eating cruciferous vegetables in all but the bromoform model. Medications did not consistently predict blood levels. Afternoon/evening blood samples had lower THM concentrations than morning samples. In a subsample ($n = 230$), air chloroform better predicted blood chloroform than water chloroform, suggesting showering/bathing was a more important source than drinking.

Conclusions: We identified several factors associated with blood THMs that may affect their metabolism. The potential health implications require further study.

Bisphenol A and Reproductive Health: Update of Experimental and Human Evidence, 2007–2013

Jackye Peretz, Lisa Vrooman, William A. Ricke, Patricia A. Hunt, Shelley Ehrlich, Russ Hauser, Vasantha Padmanabhan, Hugh S. Taylor, Shanna H. Swan, Catherine A. VandeVoort, and Jodi A. Flaws

122:775–786 (August 2014)
<http://dx.doi.org/10.1289/ehp.1307728>

Background: In 2007, an expert panel reviewed associations between bisphenol A (BPA) exposure and reproductive health outcomes. Since then, new studies have been conducted on the impact of BPA on reproduction.

Objective: In this review, we summarize data obtained since 2007, focusing on *a*) findings from human and animal studies, *b*) the effects of BPA on a variety of reproductive end points, and *c*) mechanisms of BPA action.

Methods: We reviewed the literature published from 2007 to 2013 using a PubMed search based on keywords related to BPA and male and female reproduction.

Discussion: Because BPA has been reported to affect the onset of meiosis in both animal and *in vitro* models, interfere with germ cell nest breakdown in animal models, accelerate follicle transition in several animal species, alter steroidogenesis in multiple animal models and women, and reduce oocyte quality in animal models and women undergoing *in vitro* fertilization (IVF), we consider it an ovarian toxicant. In addition, strong evidence suggests that BPA is a uterine toxicant because it impaired uterine endometrial proliferation, decreased uterine receptivity, and increased implantation failure in animal models. BPA exposure may be associated with adverse birth outcomes, hyperandrogenism, sexual dysfunction, and impaired implantation in humans, but additional studies are required to confirm these associations. Studies also suggest that BPA may be a testicular toxicant in animal models, but the data in humans are equivocal. Finally, insufficient evidence exists regarding effects of BPA on the oviduct, the placenta, and pubertal development.

Conclusion: Based on reports that BPA impacts female reproduction and has the potential to affect male reproductive systems in humans and animals, we conclude that BPA is a reproductive toxicant.

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BPA and Reproductive Health: Reviewing the Current State of the Science

Julia R. Barrett | 122:A223 (August 2014)
<http://dx.doi.org/10.1289/ehp.122-A223>

A Longitudinal Study of Urinary Phthalate Excretion in 58 Full-Term and 67 Preterm Infants from Birth through 14 Months

Hanne Frederiksen, Tanja Kuiri-Hänninen, Katharina M. Main, Leo Dunkel, and Ulla Sankilampi

122:998–1005 (September 2014)
<http://dx.doi.org/10.1289/ehp.1307569>

Background: Some phthalates have shown antiandrogenic effects in rat offspring. Premature infants may be exposed to high amounts of specific phthalates during hospitalization, and thus are potentially at risk.

Objective: We evaluated longitudinal phthalate exposure and metabolism in full-term (FT) and preterm (PT) infants.

Methods: Fifty-eight FT and 67 PT (gestational age, 24.7–36.6 weeks) infants were recruited at birth and followed until 14 months (nine times). Urinary concentrations of metabolites of diethyl phthalate (DEP), dibutyl phthalate isomers (DiBP and DnBP), butylbenzyl phthalate (BBzP), di(2-ethylhexyl) phthalate (DEHP), and diisononyl phthalate (DiNP) were measured in 894 samples. Daily intake and a hazard index for antiandrogenic effects were estimated, and excretion patterns of DEHP and DiNP metabolites were analyzed.

Results: Metabolites of BBzP, DiNP, and DEHP were 5–50 times higher at day 7 (D7) and month 1 (M1) in PT than in FT infants. Thereafter, metabolite concentrations were similar between the two groups. The estimated hazard index for combined DiBP, DnBP, BBzP, and DEHP exposures 7 days after birth exceeded the antiandrogenic threshold in > 80% of PT and > 30% of FT infants, and after M2, in 30% of all infants. The excretion pattern of DEHP and DiNP metabolites changed with age.

Conclusion: Most PT infants and approximately one-third of healthy FT newborns were exposed to phthalates during early life at a potentially harmful level according to the European Food Safety Authority's recommended limits of daily exposure. Changes in the relative proportions of secondary phthalate metabolites over time were consistent with maturation of infant metabolic pathways during the first year of life. Further research is needed on the health effects of phthalate exposures and the influence of changes in metabolic capacity in neonates and infants.

AIR POLLUTION: PARTICULATE MATTER/SMOKE/INDOOR AIR

Health and Household Air Pollution from Solid Fuel Use: The Need for Improved Exposure Assessment

Maggie L. Clark, Jennifer L. Peel, Kalpana Balakrishnan, Patrick N. Breyse, Steven N. Chillrud, Luke P. Naeher, Charles E. Rodes, Alan F. Vette, and John M. Balbus

121:1120–1128 (October 2013)
<http://dx.doi.org/10.1289/ehp.1206429>

Background: Nearly 3 billion people worldwide rely on solid fuel combustion to meet basic household energy needs. The resulting exposure to air pollution causes an estimated 4.5% of the global burden of disease. Large variability and a lack of resources for research and development have resulted in highly uncertain exposure estimates.

Objective: We sought to identify research priorities for exposure assessment that will more accurately and precisely define exposure–response relationships of household air pollution necessary to inform future cleaner-burning cookstove dissemination programs.

Data Sources: As part of an international workshop in May 2011, an expert group characterized the state of the science and developed recommendations for exposure assessment of household air pollution.

Synthesis: The following priority research areas were identified to explain variability and reduce uncertainty of household air pollution exposure measurements: improved characterization of spatial and temporal variability for studies examining both short- and long-term health effects; development and validation of measurement technology and approaches to conduct complex exposure assessments in resource-limited settings with a large range of pollutant concentrations; and development and validation of biomarkers for estimating dose. Addressing these priority research areas, which will inherently require an increased allocation of resources for cookstove research, will lead to better characterization of exposure–response relationships.

Conclusions: Although the type and extent of exposure assessment will necessarily depend on the goal and design of the cookstove study, without improved understanding of exposure–response relationships, the level of air pollution reduction necessary to meet the health targets of cookstove interventions will remain uncertain.

RELATED ARTICLES

NEWS | Take Care in the Kitchen: Avoiding Cooking-Related Pollutants

Nate Seltenrich | 122:A154 (June 2014)
<http://dx.doi.org/10.1289/ehp.122-A154>

The process of cooking food and even simply operating stoves—particularly gas appliances—can emit several potentially hazardous chemicals and compounds. Investigators suggest a few simple techniques to reduce exposure while they look for better ways to control emissions.



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EDITORIAL | Climate Change and Public Health in North Carolina: A Unique State Offers a Unique Perspective

Leah Devlin, Mikey Goralnik, William G. Ross Jr., and Kimberly Thigpen Tart | 122:A146 (June 2014)
<http://dx.doi.org/10.1289/ehp.1408542>

Long-term Exposure to PM₁₀ and NO₂ in Association with Lung Volume and Airway Resistance in the MAAS Birth Cohort

Anna Mölter, Raymond M. Agius, Frank de Vocht, Sarah Lindley, William Gerrard, Lesley Lowe, Danielle Belgrave, Adnan Custovic, and Angela Simpson

121:1232–1238 (October 2013)
<http://dx.doi.org/10.1289/ehp.1205961>

Background: Findings from previous studies on the effects of air pollution exposure on lung function during childhood have been inconsistent. A common limitation has been the quality of exposure data used, and few studies have modeled exposure longitudinally throughout early life.

Objectives: We sought to study the long-term effects of exposure to particulate matter with an aerodynamic diameter $\leq 10 \mu\text{m}$ (PM₁₀) and to nitrogen dioxide (NO₂) on specific airway resistance (sRAW) and forced expiratory volume in 1 sec (FEV₁) before and after bronchodilator treatment. Subjects were from the Manchester Asthma and Allergy Study (MAAS) birth cohort ($n = 1,185$).

Methods: Spirometry was performed during clinic visits at ages 3, 5, 8, and 11 years. Individual-level PM₁₀ and NO₂ exposures were estimated from birth to 11 years of age through a microenvironmental exposure model. Longitudinal and cross-sectional associations were estimated using generalized estimating equations and multivariable linear regression models.

Results: Lifetime exposure to PM₁₀ and NO₂ was associated with significantly less growth in FEV₁ (percent predicted) over time, both before (–1.37%; 95% CI: –2.52, –0.23 for a 1-unit increase in PM₁₀ and –0.83%; 95% CI: –1.39, –0.28 for a 1-unit increase in NO₂) and after bronchodilator treatment (–3.59%; 95% CI: –5.36, –1.83 and –1.20%; 95% CI: –1.97, –0.43, respectively). We found no association between lifetime exposure and sRAW over time. Cross-sectional analyses of detailed exposure estimates for the summer and winter before 11 years of age and lung function at 11 years indicated no significant associations.

Conclusions: Long-term PM₁₀ and NO₂ exposures were associated with small but statistically significant reductions in lung volume growth in children of elementary-school age.

Ambient Air Pollution and Preeclampsia: A Spatiotemporal Analysis

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121:1365–1371 (November–December 2013)
<http://dx.doi.org/10.1289/ehp.1206430>

Background: Available evidence concerning the association between air pollution and preeclampsia is limited, and specific associations with early- and late-onset preeclampsia have not been assessed.

Objectives: We investigated the association, if any, between preeclampsia (all, early-, and late-onset) and exposure to nitrogen dioxide, nitrogen oxides, particulate matter with aerodynamic diameter $\leq 2.5 \mu\text{m}$ (PM_{2.5}; fine particles), $\leq 10 \mu\text{m}$, and 2.5–10 μm , and PM_{2.5} light absorption (a proxy for elemental carbon) during the entire pregnancy and during the first, second, and third trimesters.

Methods: This study was based on 8,398 pregnancies (including 103 cases of preeclampsia) among women residing in Barcelona, Spain (2000–2005). We applied a spatiotemporal exposure assessment framework using land use regression models to predict ambient pollutant levels during each week of pregnancy at the geocoded residence address of each woman at the time of birth. Logistic and conditional logistic regression models were used to estimate unadjusted and adjusted associations.

Results: We found positive associations for most of our evaluated outcome–exposure pairs, with the strongest associations observed for preeclampsia and late-onset preeclampsia in relation to the third-trimester exposure to fine particulate pollutants, and for early-onset preeclampsia in relation to the first-trimester exposure to fine particulate pollutants. Among our investigated associations, those of first- and third-trimester exposures to PM_{2.5} and third-trimester exposure to PM_{2.5} absorbance and all preeclampsia, and third-trimester PM_{2.5} exposure and late-onset preeclampsia attained statistical significance.

Conclusion: We observed increased risk of preeclampsia associated with exposure to fine particulate air pollution. Our findings, in combination with previous evidence suggesting distinct pathogenic mechanisms for early- and late-onset preeclampsia, support additional research on this topic.

Pollutant Exposures from Natural Gas Cooking Burners: A Simulation-Based Assessment for Southern California

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122:43–50 (January 2014)

<http://dx.doi.org/10.1289/ehp.1306673>

Background: Residential natural gas cooking burners (NGCBs) can emit substantial quantities of pollutants, and they are typically used without venting range hoods.

Objective: We quantified pollutant concentrations and occupant exposures resulting from NGCB use in California homes.

Methods: A mass-balance model was applied to estimate time-dependent pollutant concentrations throughout homes in Southern California and the exposure concentrations experienced by individual occupants. We estimated nitrogen dioxide (NO₂), carbon monoxide (CO), and formaldehyde (HCHO) concentrations for 1 week each in summer and winter for a representative sample of Southern California homes. The model simulated pollutant emissions from NGCBs as well as NO₂ and CO entry from outdoors, dilution throughout the home, and removal by ventilation and deposition. Residence characteristics and outdoor concentrations of NO₂ and CO were obtained from available databases. We inferred ventilation rates, occupancy patterns, and burner use from household characteristics. We also explored proximity to the burner(s) and the benefits of using venting range hoods. Replicate model executions using independently generated sets of stochastic variable values yielded estimated pollutant concentration distributions with geometric means varying by < 10%.

Results: The simulation model estimated that—in homes using NGCBs without coincident use of venting range hoods—62%, 9%, and 53% of occupants are routinely exposed to NO₂, CO, and HCHO levels that exceed acute health-based standards and guidelines. NGCB use increased the sample median of the highest simulated 1-hr indoor concentrations by 100, 3,000, and 20 ppb for NO₂, CO, and HCHO, respectively.

Conclusions: Reducing pollutant exposures from NGCBs should be a public health priority. Simulation results suggest that regular use of even moderately effective venting range hoods would dramatically reduce the percentage of homes in which concentrations exceed health-based standards.

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Cooking Up Indoor Air Pollution: Emissions from Natural Gas Stoves

Wendee Nicole | 122:A27 (January 2014)

<http://dx.doi.org/10.1289/ehp.122-A27>

Enablers and Barriers to Large-Scale Uptake of Improved Solid Fuel Stoves: A Systematic Review

Eva A. Rehfuess, Elisa Puzzolo, Debbi Stanistreet, Daniel Pope, and Nigel G. Bruce

122:120–130 (February 2014)

<http://dx.doi.org/10.1289/ehp.1306639>

Background: Globally, 2.8 billion people rely on household solid fuels. Reducing the resulting adverse health, environmental, and development consequences will involve transitioning through a mix of clean fuels and improved solid fuel stoves (IS) of demonstrable effectiveness. To date, achieving uptake of IS has presented significant challenges.

Objectives: We performed a systematic review of factors that enable or limit large-scale uptake of IS in low- and middle-income countries.

Methods: We conducted systematic searches through multidisciplinary databases, specialist websites, and consulting experts. The review drew on qualitative, quantitative, and case studies and used standardized methods for screening, data extraction, critical appraisal, and synthesis. We summarized our findings as “factors” relating to one of seven domains—fuel and technology characteristics; household and setting characteristics; knowledge and perceptions; finance, tax, and subsidy aspects; market development; regulation, legislation, and standards; programmatic and policy mechanisms—and also recorded issues that impacted equity.

Results: We identified 31 factors influencing uptake from 57 studies conducted in Asia, Africa, and Latin America. All domains matter. Although factors such as offering technologies that meet household needs and save fuel, user training and support, effective financing, and facilitative government action appear to be critical, none guarantee success: All factors can be influential, depending on context. The nature of available evidence did not permit further prioritization.

Conclusions: Achieving adoption and sustained use of IS at a large scale requires that all factors, spanning household/community and program/societal levels, be assessed and supported by policy. We propose a planning tool that would aid this process and suggest further research to incorporate an evaluation of effectiveness.

Outdoor Formaldehyde and NO₂ Exposures and Markers of Genotoxicity in Children Living Near Chipboard Industries

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122:639–645 (June 2014)

<http://dx.doi.org/10.1289/ehp.1307259>

Background: Industrial air pollution is a public health hazard. Previous evidence documented increased respiratory symptoms and hospitalizations in children who live near the factories in the largest chipboard manufacturing district in Italy (Viadana).

Objectives: We evaluated the association of outdoor exposure to formaldehyde and nitrogen dioxide (NO₂) with markers of early genotoxic damage in oral mucosa cells of randomly selected children (6–12 years of age) living in Viadana.

Methods: In 2010–2011, DNA strand breaks and nuclear abnormalities were evaluated in exfoliated buccal cells by the comet and micronucleus assays, respectively, and formaldehyde and NO₂ were monitored by passive sampling. Annual exposure estimates to pollutants were assigned to children's houses by spatial interpolation.

Results: Of 656 children, 413 (63%) participated. Children living near (< 2 km) the chipboard industries had the highest average exposure to formaldehyde and NO₂ ($p < 0.001$). A 1-SD increase in formaldehyde (0.20 µg/m³) was associated with a 0.13% (95% CI: 0.03, 0.22%) higher comet tail intensity, a 0.007 (95% CI: 0.001, 0.012) higher tail moment, and a 12% relative increase [relative risk (RR) = 1.12; 95% CI: 1.02, 1.23] in nuclear buds. A 1-SD NO₂ increase (2.13 µg/m³) was associated with a 0.13% (95% CI: 0.07, 0.19%) increase in binucleated cells and a 16% relative increase (RR = 1.16; 95% CI: 1.06, 1.26) in nuclear buds.

Conclusions: Exposure to pollutants was associated with markers of genotoxicity in exfoliated buccal cells of children living in a region with chipboard industries. These findings, combined with previously reported associations between chipboard industrial activities and respiratory outcomes in children, add to concerns about potential adverse effects of industry-related exposures in the Viadana district.

RADIATION

Guidelines for Exposure Assessment in Health Risk Studies Following a Nuclear Reactor Accident

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122:1–5 (January 2014)

<http://dx.doi.org/10.1289/ehp.1307120>

Background: Worldwide concerns regarding health effects after the Chernobyl and Fukushima nuclear power plant accidents indicate a clear need to identify short- and long-term health impacts that might result from accidents in the future. Fundamental to addressing this problem are reliable and accurate radiation dose estimates for the affected populations. The available guidance for activities following nuclear accidents is limited with regard to strategies for dose assessment in health risk studies.

Objectives: Here we propose a comprehensive systematic approach to estimating radiation doses for the evaluation of health risks resulting from a nuclear power plant accident, reflected in a set of seven guidelines.

Discussion: Four major nuclear reactor accidents have occurred during the history of nuclear power production. The circumstances leading to these accidents were varied, as were the magnitude of the releases of radioactive materials, the pathways by which persons were exposed, the data collected afterward, and the lifestyle factors and dietary consumption that played an important role in the associated radiation exposure of the affected populations. Accidents involving nuclear reactors may occur in the future under a variety of conditions. The guidelines we recommend here are intended to facilitate obtaining reliable dose estimations for a range of different exposure conditions. We recognize that full implementation of the proposed approach may not always be feasible because of other priorities during the nuclear accident emergency and because of limited resources in manpower and equipment.

Conclusions: The proposed approach can serve as a basis to optimize the value of radiation dose reconstruction following a nuclear reactor accident.

Assessment of the Risk of Medium-Term Internal Contamination in Minamisoma City, Fukushima, Japan, after the Fukushima Dai-ichi Nuclear Accident

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122:587–593 (June 2014)
<http://dx.doi.org/10.1289/ehp.1306848>

Background: The Fukushima Dai-ichi nuclear disaster, the first level-7 major nuclear disaster since Chernobyl, raised concerns about the future health consequences of exposure to and intake of radionuclides. Factors determining the risk and level of internal radiation contamination after a nuclear accident, which are a key to understanding and improving current nuclear disaster management, are not well studied.

Objective: We investigated both the prevalence and level of internal contamination in residents of Minamisoma, and identified factors determining the risk and levels of contamination.

Methods: We implemented a program assessing internal radiation contamination using a whole body counter (WBC) measurement and a questionnaire survey in Minamisoma, between October 2011 and March 2012.

Results: Approximately 20% of the city's population (8,829 individuals) participated in the WBC measurement for internal contamination, of which 94% responded to the questionnaire. The proportion of participants with detectable internal contamination was 40% in adults and 9% in children. The level of internal contamination ranged from 2.3 to 196.5 Bq/kg (median, 11.3 Bq/kg). Tobit regression analysis identified two main risk factors: more time spent outdoors, and intake of potentially contaminated foods and water.

Conclusions: Our findings suggest that, with sensible and reasonable precautions, people may be able to live continuously in radiation-affected areas with limited contamination risk. To enable this, nuclear disaster response should strictly enforce food and water controls and disseminate evidence-based and up-to-date information about avoidable contamination risks.

» NEWS | SCIENCE SELECTION

Data for Disaster Planning: Risk Factors for Internal Radiation Exposures after Fukushima

Lindsey Konkel | 122:A166 (June 2014)
<http://dx.doi.org/10.1289/ehp.122-A166>

RELATED ARTICLES

NEWS | Once Upon a Mine: The Legacy of Uranium on the Navajo Nation

Carrie Arnold | 122:A44 (February 2014)
<http://dx.doi.org/10.1289/ehp.122-A44>

The Navajo Nation is home to hundreds of abandoned uranium mines, ranging from small holes dug by a single prospector into the side of a mesa to large commercial mining operations. Within decades of the arrival of prospectors in the 1940s, Navajo miners were being diagnosed with lung cancer, a relatively rare disease in this largely nonsmoking population. Today the Navajo population remains at high risk for kidney disease as a result of uranium exposure, as well as potentially associated hypertension, cardiovascular disease, and autoimmune diseases.



NEWS | Urban Gardening: Managing the Risks of Contaminated Soil

Rebecca Kessler | 121:A326 (November–December 2013)
<http://dx.doi.org/10.1289/ehp.121-A326>

The urban decay of the middle and late twentieth century has given way to a gardening revival in cities around the globe. But urban soils are often heavily contaminated with metals, polycyclic aromatic hydrocarbons, and other contaminants, prompting questions about the health consequences of urban gardening—and some new solutions.

Methodologies and Populations

EPIGENETICS, EXPOSOME, BIOMARKERS

The Human Early-Life Exposome (HELIX): Project Rationale and Design

Martine Vrijheid, Rémy Slama, Oliver Robinson, Leda Chatzi, Muireann Coen, Peter van den Hazel, Cathrine Thomsen, John Wright, Toby J. Athersuch, Narcis Avellana, Xavier Basagaña, Celine Brochot, Luca Bucchini, Mariona Bustamante, Angel Carracedo, Maribel Casas, Xavier Estivill, Lesley Fairley, Diana van Gent, Juan R. Gonzalez, Berit Granum, Regina Gražulevičienė, Kristine B. Gutzkow, Jordi Julvez, Hector C. Keun, Manolis Kogevinas, Rosemary R.C. McEachan, Helle Margrete Meltzer, Eduard Sabido, Per E. Schwarze, Valérie Siroux, Jordi Sunyer, Elizabeth J. Want, Florence Zeman, and Mark J. Nieuwenhuijsen

122:535–544 (June 2014)

<http://dx.doi.org/10.1289/ehp.1307204>

Background: Developmental periods in early life may be particularly vulnerable to impacts of environmental exposures. Human research on this topic has generally focused on single exposure–health effect relationships. The “exposome” concept encompasses the totality of exposures from conception onward, complementing the genome.

Objectives: The Human Early-Life Exposome (HELIX) project is a new collaborative research project that aims to implement novel exposure assessment and biomarker methods to characterize early-life exposure to multiple environmental factors and associate these with omics biomarkers and child health outcomes, thus characterizing the “early-life exposome.” Here we describe the general design of the project.

Methods: In six existing birth cohort studies in Europe, HELIX will estimate prenatal and postnatal exposure to a broad range of chemical and physical exposures. Exposure models will be developed for the full cohorts totaling 32,000 mother–child pairs, and biomarkers will be measured in a subset of 1,200 mother–child pairs. Nested repeat-sampling panel studies ($n = 150$) will collect data on biomarker variability, use smartphones to assess mobility and physical activity, and perform personal exposure monitoring. Omics techniques will determine molecular profiles (metabolome, proteome, transcriptome, epigenome) associated with exposures. Statistical methods for multiple exposures will provide exposure–response estimates for fetal and child growth, obesity, neurodevelopment, and respiratory outcomes. A health impact assessment exercise will evaluate risks and benefits of combined exposures.

Conclusions: HELIX is one of the first attempts to describe the early-life exposome of European populations and unravel its relation to omics markers and health in childhood. As proof of concept, it will form an important first step toward the life-course exposome.

» NEWS | SCIENCE SELECTION

The HELIX Project: Tracking the Exposome in Real Time

Carol Potera | 122:A169 (June 2014)

<http://dx.doi.org/10.1289/ehp.122-A169>

Micronuclei in Cord Blood Lymphocytes and Associations with Biomarkers of Exposure to Carcinogens and Hormonally Active Factors, Gene Polymorphisms, and Gene Expression: The NewGeneris Cohort

Domenico Franco Merlo, Silvia Agramunt, Livia Anna, Harrie Besselink, Maria Botsivali, Nigel J. Brady, Marcello Ceppi, Leda Chatzi, Bowang Chen, Ilse Decordier, Peter B. Farmer, Sarah Fleming, Vincenzo Fontana, Asta Försti, Eleni Fthenou, Fabio Gallo, Panagiotis Georgiadis, Hans Gmuender, Roger W. Godschalk, Berit Granum, Laura J. Hardie, Kari Hemminki, Kevin Hochstenbach, Lisbeth E. Knudsen, Manolis Kogevinas, Katalin Kovács, Soterios A. Kyrtopoulos, Martinus Løvik, Jeanette K Nielsen, Unni Cecilie Nygaard, Marie Pedersen, Per Rydberg, Bernadette Schoket, Dan Segerbäck, Rajinder Singh, Jordi Sunyer, Margareta Törnqvist, Henk van Loveren, Frederik J. van Schooten, Kim Vande Look, Hans von Stedingk, John Wright, Jos C. Kleinjans, Micheline Kirsch-Volders, Joost H.M. van Delft, and the NewGeneris Consortium

122:193–200 (February 2014)

<http://dx.doi.org/10.1289/ehp.1206324>

Background: Leukemia incidence has increased in recent decades among European children, suggesting that early-life environmental exposures play an important role in disease development.

Objectives: We investigated the hypothesis that childhood susceptibility may increase as a result of *in utero* exposure to carcinogens and hormonally acting factors. Using cord blood samples from the NewGeneris cohort, we examined associations between a range of biomarkers of carcinogen exposure and hormonally acting factors with micronuclei (MN) frequency as a proxy measure of cancer risk. Associations with gene expression and genotype were also explored.

Methods: DNA and protein adducts, gene expression profiles, circulating hormonally acting factors, and GWAS (genome-wide association study) data were investigated in relation to genotoxic damage measured by MN frequency in lymphocytes from 623 newborns enrolled between 2006 and 2010 across Europe.

Results: Malondialdehyde DNA adducts (M_1dG) were associated with increased MN frequency in binucleated lymphocytes (MNBN), and exposure to androgenic, estrogenic, and dioxin-like compounds was associated with MN frequency in mononucleated lymphocytes (MNMNO), although no monotonic exposure–outcome relationship was observed. Lower frequencies of MNBN were associated with a 1-unit increase expression of *PDCD11*, *LATS2*, *TRIM13*, *CD28*, *SMC1A*, *IL7R*, and *NIPBL* genes. Gene expression was significantly higher in association with the highest versus lowest category of bulky and M_1dG –DNA adducts for five and six genes, respectively. Gene expression levels were significantly lower for 11 genes in association with the highest versus lowest category of plasma AR CALUX® (chemically activated luciferase expression for androgens) (8 genes), ERα CALUX® (for estrogens) (2 genes), and DR CALUX® (for dioxins). Several SNPs (single-nucleotide polymorphisms) on chromosome 11 near *FOLH1* significantly modified associations between androgen activity and MNBN frequency. Polymorphisms in *EPHX1/2* and *CYP2E1* were associated with MNBN.

Conclusion: We measured *in utero* exposure to selected environmental carcinogens and circulating hormonally acting factors and detected associations with MN frequency in newborns circulating T lymphocytes. The results highlight mechanisms that may contribute to carcinogen-induced leukemia and require further research.

Methodologies and Populations

METHODOLOGIES

A Unique Co-culture Model for Fundamental and Applied Studies of Human Fetoplacental Steroidogenesis and Interference by Environmental Chemicals

Andrée-Anne Hudon Thibeault, Kathy Deroy, Cathy Vaillancourt, and J. Thomas Sanderson

122:371–377 (April 2014)

<http://dx.doi.org/10.1289/ehp.1307518>

Background: Experimental tools for studying the complex steroidogenic interactions that occur between placenta and fetus during human pregnancy are extremely limited.

Objectives: We aimed to develop a co-culture model to study steroidogenesis by the human fetoplacental unit and its disruption by exposure to environmental contaminants.

Methods: We cultured BeWo human choriocarcinoma cells, representing the villous cytotrophoblast, and H295R human adrenocortical carcinoma cells, representing the fetal unit, in a carefully adapted co-culture medium. We placed H295R cells in 24-well plates and BeWo cells on transwell inserts with or without pesticide treatment (atrazine or prochloraz) and assessed CYP19 activity and hormonal production after 24 hr of co-culture.

Results: The co-culture exhibited the steroidogenic profile of the fetoplacental unit, allowing a synergistic production of estradiol and estriol (but not of estrone) of 133.3 ± 11.3 pg/mL and 440.8 ± 44.0 pg/mL, respectively. Atrazine and prochloraz had cell-type specific effects on CYP19 activity and estrogen production in co-culture. Atrazine induced CYP19 activity and estrogen production in H295R cells only, but did not affect overall estrogen production in co-culture, whereas prochloraz inhibited CYP19 activity exclusively in BeWo cells and reduced estrogen production in co-culture by almost 90%. In contrast, prochloraz did not affect estradiol or estrone production in BeWo cells in monoculture. These differential effects underline the relevance of our co-culture approach to model fetoplacental steroidogenesis.

Conclusions: The co-culture of H295R and BeWo cells creates a unique *in vitro* model to reproduce the steroidogenic cooperation between fetus and placenta during pregnancy and can be used to study the endocrine-disrupting effects of environmental chemicals.

RELATED ARTICLE

NEWS | Uncertain Inheritance: Transgenerational Effects of Environmental Exposures

Charles W. Schmidt | 121:A298 (October 2013)
<http://dx.doi.org/10.1289/ehp.121-A298>

Animal studies have reported transgenerational effects for chemicals including permethrin, DEET, bisphenol A, a number of phthalates, dioxin, jet fuel mixtures, nicotine, and tributyltin, among others. Although no human data yet exist for effects to the F₃ generation, several studies have documented multigenerational chemical impacts, and the new findings are spurring a reevaluation of how scientists perceive environmental health threats.



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